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Meeting of:

PANEL ON

OPHTHALMIC DEVICES

OPEN SESSION

July 23, 1999

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P R O C E E D I N G S (8:15 a.m.)

AGENDA ITEM: Call to Order, Introductory Remarks.

DR. MC CULLEY: I want to call to order the Ophthalmic Device Panel meeting of July 23, 1999. I will turn the floor to Sarah Thornton.

MS. THORNTON: Good morning, and welcome to everyone. Before we go on with today's agenda, I will make the same few short announcements that I made yesterday.

I would like to remind everyone that you are requested to sign in on the attendance sheets in the registration area, just outside the meeting room.

You can pick up an agenda there, and information about today's meeting and how to obtain summary minutes or panel transcripts after the minutes.

Please make a note that there is a panel meeting tentatively scheduled for September 23, 1999. Stay tuned to our web site.

I think probably in the next week or two there will be further information on that meeting.

Messages for the panel members and FDA participants, information or special needs should be directed through Ms. Anne Marie Williams or Ms. Theresa Lewis, who are available at the registration table.

This is Anne Marie Williams right here. She will

be able to help you, I am sure.

For those of you with cell phones and pagers, we ask that you turn them off or put them on the vibration mode, so as not to disturb the panel or anyone making presentations.

I wanted to note, for the folks who are going to be presenting, that there are name tents on the table. This is for FDA staff. Just pick out whichever name you like, and you can put it up while you are presenting, but they are over there on the table for you.

Please, speak into the microphone and give your name clearly. This applies mostly to panel members, but also to anyone who is making presentations.

It is very important for us to have accurate reporting, as well as the correct name with the correct comment.

I would like now to extend a special welcome to our panel for the second day, and to express FDA's appreciation for the time they have taken from their schedules to prepare for this meeting. We truly appreciate it.

Please introduce yourselves for the record, panel, beginning with Dr. Yarros.

DR. YARROS: Marcia Yarros, director of regulatory

affairs for Allergan in Irvine, California, and industry representative to the panel.

MS. MORRIS: I am Lynn Morris with the state department of consumer affairs in California.

DR. FERRIS: Frederick Ferris, director of the division of biometry and epidemiology, National Eye Institute.

DR. VAN METER: Woodford Van Meter, private practice in cornea and external disease in Lexington, Kentucky.

DR. MACSAI: Miriam Macsai, professor of ophthalmology, West Virginia University School of Medicine.

DR. JURKUS: Janice Jurkus, professor of optometry, Illinois College of Optometry.

DR. HIGGINBOTHAM: Eve Higginbotham, professor and chair, department of ophthalmology, University of Maryland School of Medicine.

DR. PULIDO: Jose Pulido, professor and head, department of ophthalmology, University of Illinois.

DR. MC CULLEY: Jim McCulley, department of ophthalmology, University of Texas Southwestern Medical School.

DR. SUGAR: Joel Sugar, professor and vice chair, department of ophthalmology, University of Illinois at

Chicago.

DR. BULLIMORE: Mark Bullimore, associate professor, The Ohio State University College of Optometry.

DR. GRIMMETT: Michael Grimmett, assistant professor, department of ophthalmology, University of Miami School of Medicine.

DR. MATOBA: Alice Matoba, associate professor of ophthalmology, Baylor College of Medicine.

DR. MANNIS: Mark Mannis, professor of ophthalmology, University of California, Davis.

DR. WANG: Ming Wang, director of refractory surgery, Vanderbilt University.

DR. ROSENTHAL: Ralph Rosenthal, director of the division of ophthalmic devices.

MS. THORNTON: Thank you. I would like to read the conflict of interest statement for the ophthalmic devices panel meeting for July 23, 1999.

The following announcement addresses conflict of interest issues associated with this meeting and is made part of the record to preclude even the appearance of an impropriety.

To determine if any conflict existed, the agency reviewed the submitted agenda and all financial interests reported by the committee participants.

The conflict of interest statutes prohibit special government employees from participating in matters that could affect their or their employers financial interests.

However, the agency has determined that participation of certain members and consultants, the need for whose services outweigh the potential conflict of interest involved, is in the best interests of the government.

Waivers are on file for Drs. Woodford Van Meter and James McCulley, and waivers have also been granted for Drs. Eve Higginbotham, Jose Pulido and Ming Wang, for their interests in firms that could potentially be affected by the panel's deliberations.

The waivers allow these individuals to participate fully in the panel's deliberations. Copies of these waivers may be obtained from the agency's Freedom of Information Office, Room 12-A-15 of the Parklawn Building.

We would like to note for the record that the agency took into consideration certain matters regarding Drs. Mark Bullimore, Frederick Ferris, Eve Higginbotham, Janice Jurkus, Marianne Macsai, Mark Mannis, James McCulley and Ming Wang.

These individuals reported past and/or current interests in firms at issue, but in matters not related to

the specific issues of today's agenda.

Therefore, the agency has determined that they may fully participate today. The agency also considered Drs. Michael Grimmett's and Mark Mannis' reported involvements related to vision correction.

In the absence of any financial interests, the agency has determined that they may participate fully in today's deliberations.

In the event that the discussions involve any other products or firms not already on the agenda, for which an FDA participant has a financial interest, the participant should excuse him or herself from such involvement, and the exclusion will be noted for the record.

With respect to all other participants, we ask, in the interests of fairness, that all persons making statements or presentations disclose any current or previous financial involvement with any firm they may wish to comment upon.

I would like to now read the appointment to temporary voting status.

Pursuant to the authority granted under the Medical Devices Advisory Committee charter, dated October 27, 1990, as amended April 20, 1995 and October 10, 1997, I appoint the following individuals as voting members of the

ophthalmic devices panel for the duration of this meeting on July 23, 1999:

Drs. Frederick Ferris, Mark Mannis, Woodford Van Meter, Alice Matoba and Ming Wang.

I also appoint Dr. Michael Grimmett as a voting member of the panel for the discussion of the intraocular lens for the correction of aphakia.

For the record, these persons are special government employees and are consultants to this panel or consultants or voting members of another panel under the Medical Devices Advisory Committee.

They have undergone the customary conflict of interest review and have reviewed the material to be considered at this meeting.

This is signed, Dr. David W. Feigel, Jr., director, Center for Devices and Radiological Health, July 21, 1999. Thank you, Dr. McCulley.

DR. MC CULLEY: Thank you. Just to add a new, so everyone knows up front, a new wrinkle to how we are doing business, we follow an agenda in the program that gives us an order of the things to do, and in some situations, the time frame within which it must be done, which we read and follow, or I read and we follow.

There has been one addition. That is, one of the

primary reviewers will serve as scribe during the primary reviews, to list all the concerns that come up, so that we have those very well recorded, so I am not trying to do two or three things at once.

I am going to ask that Dr. Van Meter be the scribe this morning and Dr. Sugar the scribe this afternoon. Also, I won't go through everything I did yesterday, but everyone please remain aware of not only real conflict of interest, but the perception of conflict of interest, which can be drawn potentially in the minds of some people, if individuals are seen pow-wowing during the course of the meeting.

We must keep our comments on PMAs to ourselves and not discuss them with anyone in the audience or with ourselves.

With that, I would like to open the public hearing session of this meeting. Thirty minutes is allocated for public hearing, where members of the public may come forward and speak.

Each individual is limited to no more than 10 minutes. We have one person who has requested time prior to the meeting, Dr. William Bond.

AGENDA ITEM: Open Public Hearing.

DR. BOND: Thank you, Mr. Chairman. I am William

Bond. I am an ophthalmologist in central Illinois. I am speaking for, this afternoon, the Summit Apex-Plus Laser, for the approval of LASIK. I have some prepared remarks.

As a Summit CRS investigator core study, I would like to respectfully submit to the panel the following points in support of labeling the Summit Apex-Plus Laser for LASIK.

LASIK is currently the true standard of care for refractive surgery in the United States and elsewhere. Extensive studies, including the CRS study, have proven LASIK on a Summit laser to be safe and effective.

DR. MC CULLEY: Excuse me. I hate to interrupt you, but I need for you please to state whether you have any conflicts of interest, who paid your way here, and things of that sort.

DR. BOND: I paid my own way here, missed a day and a half of work, and I own a Summit laser. I am out on this quite a bit.

DR. MC CULLEY: No accusations, just that we need it for the record, and it was pointed out to me that we hadn't gotten it.

DR. BOND: I am sorry. I own a Summit laser. Other than that, I am on my own.

Accuracy in labeling serves the entire public, not

just the MDs and the laser manufacturers but, most of all, the patients.

LASIK is by far the most commonly performed refractive procedure on all eximer lasers, including the Summit Apex Plus.

This is because the surgeons actually treating the patients have found LASIK to be safe, effective, reliable and reproducible.

The laser should be approved and labeled for its most common actual use, and the use shown to be preferred by both doctors and patients.

Labeling the Summit Apex Plus laser for LASIK allows the LASIK procedure to be done in a manner best serving the public.

American patients should have access to the best LASIK software. Currently, better software for such things as central island prevention and multiple zones -- to give two examples of many -- is unavailable to the majority of the American public, although freely available outside the USA.

On-label LASIK would eliminate such unscientific, but politically mandated maneuvers such as double carding.

In my own experience with both the Summit Apex and the Summit Apex Plus laser, CRS software gives better

results than the approved PRK software.

Regulations originally meant to protect patients wind up obstructing care, as knowledge and circumstances change.

For instance, I cannot access very low amounts of myopia in my Summit Apex Plus laser, which would be of great benefit to certain patients, particularly in enhancement situations.

These useful myopic instruments are not unavailable due to lack of engineering skill or scientific knowledge, but by decree, and not very recent decree.

The public is best served by frank talk among MDs. One of the things about my profession of which I have been the proudest has been the absolute free exchange of medical knowledge among doctors, exemplified by the remark, there are no secrets in medicine.

Ideas, results, concepts, techniques are shared freely for the benefits of everyone's patients. It is a wonderful tradition.

There is also a place for free and frank exchange between MDs and laser manufacturers, perhaps leading to advances in design.

Due to regulation, perhaps over-interpretation of regulation, we now often find ourselves in a Kafka-esque

world of circumlocution, code words, particularly with manufacturers. On label LASIK would eliminate this unhealthy situation.

Not everyone here is a surgeon, but we are all patients. The interests of patients very rightly take precedence over all other considerations, but I would still like to mention a few issues that concern MDs directly.

On label LASIK is a direct benefit to MDs, because it resolves certain issues with professional liability insurance, which in turn affects cost of, and access to medical care.

Insurance companies prefer premiums to claims, and especially seem to dislike the claims on which they have to pay out.

LASIK is the established standard of care refractive procedure. An insurance carrier or plaintiff's attorney should not be able to deem LASIK experimental.

It is a lamentable state of affairs when a surgeon has to describe to the patient the most commonly done, safe and effective refractive procedure as off label, not approved by the FDA, investigational, experimental.

It is no longer the last two of these two, and should no longer be the first two. I thank you for your kind attention.

DR. MC CULLEY: Thank you. Does the panel have any questions for Dr. Bond? Seeing none, we thank you for your comments.

Time allows, if there are others in the audience who wish to come forward and make comment. Seeing none, we will close the open public hearing. The open committee discussions will begin with branch updates. Dr. Rosenthal?

AGENDA ITEM: Open Committee Discussion. Branch Updates.

DR. SAVIOLA: I believe I am first on the agenda. Good morning. My name is Dr. Jim Saviola. I am chief of the vitreoretinal and extraocular devices branch in the division.

For the record, I am a government employee. I am restricted, so I have no financial interests in any of the topics discussed today.

There are three topics I would like to update the panel on. The first deals with the standards recognition process.

Last week, on July 12, the agency published in the Federal Register a notification of the modifications to the list of recognized standards used in the premarket review standards.

Added to the list of recognized ophthalmic

standards was the American National Standards Institute ANSI Z.80.20, 1998, titled, Ophthalmics, contact lenses, standard terminology, tolerances, measurements and physicochemical properties.

This standard was completely recognized, with four exceptions that are summarized on the supplementary information sheet for the standard.

More complete information regarding the details can be found on our CDRH web site. The standards recognition process was addressed in the FDA Modernization Act of 1997, as a way to allow the agency to recognize consensus standards for use in satisfying portions of device submissions.

The list of standards is published at least once a year. In the contact lens area, previously there were 13 standards recognized that were developed by the International Standards Organization, ISO, that pertained to some aspect of contact lenses or care products.

This ANSI Z.80.20 standard was available as of last Monday for manufacturers to use as part of their submissions process.

A second item with regard to PMA approval, on February 5, 1999, the FDA approved the Bausch and Lomb pure vision soft contact lens for seven-day extended wear for

aphakic or non-aphakic persons.

This lens is manufactured from a silicon hydrogel material. The generic name is balfilcon A.

The company is marketing the lens overseas as well as in the United States.

Since this was a seven-day indication for extended wear, it was not reviewed by the ophthalmic devices advisory panel.

The last item, back in October 1998, I had updated the panel about the health notification on the illegal promotion of orthokeratology contact lenses and tinted lenses, dated September 25, 1998.

While there is still one daily or orthokeratology lens, the Contex OK lens that is cleared for marketing, there are now two companies that have received a marketing clearance for their after-market lens tinting service.

The first company cleared was Adventures in Colors, that offers a tinting process for lenses that have already been prescribed for patients by a practitioner.

The second company, Colorsoft Laboratories, has also received a similar marketing clearance.

Adventures in Color has also received a second 510(k) clearance for a prosthetic tinted lens. Our branch is continuing to work with other lens tinting services to

help them meet their regulatory requirements.

That concludes my updates. Are there any questions?

DR. MC CULLEY: Seeing none, I guess we are going to go down the order.

DR. BEERS: Hi. I am Everette Beers. I am acting branch chief today for Morris Waxler, who you saw here yesterday. This is update for the diagnostic and surgical devices branch.

I wanted to thank the members of the branch and the other branches in the division and members of the statistics team, for the continued high quality of scientific review and team leading.

Within the diagnostic and surgical devices branch, I wanted to thank Ms. Quynh Hoang, Ms. Jan Callaway, Ms. Marsha Nicholas, Ms. Daryl Kaufman, Mr. Denis McCarthy, and Dr. Bruce Drum.

From the division, Dr. Bernie Lepri, Dr. Malvina Eydelman, Dr. Sheryl Berman, Dr. Ralph Rosenthal and Ms. Deborah Falls.

From the other two branches, the intraocular and corneal implant branch, and the vitreoretinal and extraocular devices branch, who have helped out our branch in team leading some of our IDEs and PMAs, I wanted to thank

Ms. Ming Shih, Ms. Karen Warburton, Ms. Sue Jones, and Dr. Kesia Alexander.

In updates from previous meetings of the panel, the PMA P970001, which is the Emery Vision correction PMA for refractive surgery for myopic using LASIK, that PMA remains under review.

The guidance document that was referred to yesterday for refractive surgical lasers, and as Dr. Rosenthal and Dr. Waxler mentioned, that has not been revised.

That is the October 10, 1996 guidance entitled, Checklist of Information Usually Submitted in an Investigational Device Exemptions Application for Refractive Surgery Lasers. That is up on the web site, on the CDRH web site.

I wanted to touch on our submissions that we have received in the last 12 months. PMA submissions, we received four original PMAs.

Then, 24 PMA supplements and amendments from 11 manufacturers, covering 13 PMAs.

For IDEs, we had 542 IDE submissions. That includes 212 submissions from manufacturers covering six original IDEs and 206 amendments and supplements.

The remaining 330 IDE submissions were from

sponsor investigators, 12 original IDEs and 318 amendments and supplements.

For 510(k) -- that is premarket notification submissions -- we had 96 510(k)s. Almost 20 percent of those 510(k)s were for keratomes.

That concludes the DSDB. Are there any questions from the panel?

DR. MC CULLEY: How many of those were for keratomes?

DR. BEERS: Actually, around 19 percent of the 96, so we had about 17.

DR. MC CULLEY: Thank you. Any other questions for Dr. Beers? Okay.

DR. BOULWARE: Good morning. I am Ashley Boulware, currently acting branch chief for the intraocular and corneal devices branch.

I am pleased to announce we have two PMAs that have been approved since the last panel meeting, P960033, Staar Surgical, Staar Visolasik was approved on July 2, 1999. This was a non-panel track document.

P980031, the KeraVision Intacs, were approved on April 9, 1999.

We are pleased to announce that the accountability analysis for clinical studies of ophthalmic devices advice

document was issued in early May as a draft guidance document and is available on the web, and there are also copies on the table outside this room.

We are currently in the 90-day comment period, and comments will be considered prior to a final guidance being issued.

We have also released an updated draft of our guidance for intraocular lenses. This was posted on the FDA web site on Friday, July 16.

The Federal Register notice should issue within the next four to six weeks. Following the release of the Federal Register notice, there will be a 90-day comment period before the document will be released in final form.

We would encourage panel members, industry members and interested members of the public to submit their comments. The address for comments can be found on the second page of the guidance document.

Changes from the last draft include the inclusion of the updated grid, which was compiled based on panel recommendations.

The only change to the grid from the panel discussion at the October 1997 meeting is in the presentation of the total visual acuity rates.

In the Stark Grid, the older grid, the total

visual acuity rates were calculated assuming an equal distribution of subjects in each age subgroup -- 60 to 69, 70 to 79, et cetera.

In the updated grid, the total VA rates represent the rates associated with the distribution of subjects in the four age subgroups found in the historical control data.

So, for a clinical study with different age distributions of subjects, the age-adjusted total control rate should be calculated from a weighted average of the age subgroup rates in the study. This becomes a little more obvious when you see the tables and the annex to the guidance document.

Finally, I wanted to mention that keratoprosthesis and aqueous shunts, which were both pre-amendment devices, or devices that were on the market prior to 1976, SMDA90 instructed the agency to either call for PMAs for these devices or reclassify these devices.

Following an analysis of data submitted in response to a 515(i) or a call for information, a Federal Register notice issued on March 15, 1999, proposing to reclassify both keratoprosthesis and aqueous shunts for glaucoma from class III to class II.

Final guidance documents for both devices have also been issued, and are proposed to serve as special

controls.

The comment period ended on June 14, 1999, and the comments will be considered and addressed when the final rule is issued in the Federal Register. This concludes my branch update. Are there any questions?

DR. MC CULLEY: Seeing none, we thank you.

We will now begin deliberation on PMA P990014. We would like to invite the sponsors forward for 60 allotted minutes to present your PMA.

AGENDA ITEM: PMA #P990014.

DR. WALKER: Good morning. My name is Melissa Walker and I am responsible for regulatory affairs for Bausch and Lomb Surgical, and I will be giving you a background on the product you are going to be reviewing today, as well as introducing the other speakers.

A little background on the company, we are a division of Bausch and Lomb, Incorporated. We were formed in December of 1997 as a result of the purchase of Chiron Vision and Storz Ophthalmics and a subsequent merger.

We market products including intraocular lenses, viscoelastics, phakoemulsification equipment, accessories, refractive lasers and accessories, as well as ophthalmic instrumentation.

Today we are seeking approval of intraocular lens

model H60M. It is a composite hydrogel PMMA one-piece lens.

There are almost half a million lenses marketed since 1995, and it is currently sold in 36 international markets. These are manufactured in our Clearwater, Florida facility.

The data that will be reviewed for you today will be from the IDE study that was initiated in 1995. There were a total of 21 investigators who enrolled 387 patients.

Also, you will hear a summary of a PC Haze substudy that was initiated in 1996 at the agency's request. It included three lens models, the one-piece PMMA, the H60M, and a three-piece silicon model. There were 100 patients per lens model.

The 100 H60M subjects that were in the substudy are also included in the core study results.

Presenters today are Dr. George Green, who is the director of implant research and development for Bausch and Lomb Surgical. He will review the design, the material and some manufacture of the Hydroview lens.

Dr. Douglas Koch, from Baylor College of Medicine, will review the clinical study results. Dr. Patrick O'Meara will be available to answer questions on data analysis for the studies.

DR. GREEN: Good morning. I am George Green, the

director of implant research and development at Bausch and Lomb.

I am here today to review briefly the lens model, the subject of this PMA.

The lens is the H60M. It is a posterior chamber, one-piece intraocular lens. It is of a composite construction. It has a hydrogel optic and PMMA haptics.

As you can see here, it has a full six millimeter flare optic, and it is 12.5 millimeters in overall length.

The optic material is composed of a hydrogel of 2-hydroxyethylmethacrylate, or hema, and 6-hydroxyhexamethacrylate, called hexema.

This material is cross linked with hexanediodimethacrylate, and a benzotriazol-type acrylate bondable UF absorber is incorporated into the optic.

The PMMA haptic is composed of methylmethacrylate cross linked with ethylene glycoldimethacrylate, and colored blue with DNC green number 6.

This optic, as mentioned, is a full six millimeters in diameter. It is an equal biconvex design, is an 18 percent water content hydrogel, and has a refractive index of 1.474.

The blue colored hema haptics are of a modified C-loop designed, effective angle is 6.1 degrees. As mentioned

before, it has a 12.5 millimeter overall length.

This lens is manufactured by first casting a composite rod from which the lens will be machined. The optic is manufactured by combining the monomers previously mentioned, dispensing into molds, curing at an elevated temperature and then machining to the six millimeter diameter.

The surrounding PMMA is cast by centering these four rods into molds, and dispensing the blue-colored methylmethacrylate around them, curing it at elevated temperature.

The intraocular lens is manufactured as any other one-piece intraocular lens would be made. The composite rods here are sliced into discs. The IOL is cut from the disc as a one-piece lens.

The disc is lathed on both sides. The haptic shape and optic diameter are cut by CNC mill. The lenses are hydrated, polished, inspected and sterilized.

I have a brief one-minute video to show you this manufacturing process.

[Video is shown.]

You can see here, this is the composite rod. It is then inserted, it is machined, it is sliced into discs. The discs are measured.

What is shown here is the disc about ready to be machined, showing the clear optic center and the clear PMMA surrounding.

The disc is lathe cut, anterior side, and then posterior side. This is a machining operation as any other single piece lens is manufactured in our manufacturing plant in Clearwater.

The second side is lathe cut again, identical to a one-piece LPMMA lens. Here we see the mill as it begins to cut the haptic shape and the optic diameter. From this point, it is a hard lens.

It is removed, and it goes through the hydration and polishing process.

Prior to the IDE study, an extensive battery of biocompatability tests, meeting both the ANSI and ISO standards was performed on these lenses, and it passed all of these tests.

Extensive power stability has been performed upon this hydrogel optic. Shelf life testing has shown that aging does not affect the lens power of this particular lens.

We performed three-year accelerated aging; we have 21-month real-time aging. We also have additional studies of a combination of accelerated and real time aging for four

and 7.5 years, showing no change in the optic power of this material.

This lens has basically one method of recommended folding. Although it has a couple of iterations on how it is achieved, the lens should be folded on the 12:00 to 6:00 o'clock axis.

For the IDE, we had what was called an Ultem holder, which was merely a device which protected the lens during sterilization and shipping.

The lens was folded using multiple folding instruments. We recommended two particular instruments, an osher cyberfolder and a hydrofolder.

It was then grasped with the lens inserter of the surgeon's choice and inserted into the eye.

We have also incorporated into this PMA a new system called the Surefold, which is a holder and folder combined.

This system ensures the correct folding axis. Again, this is not an inserter. It is merely a folding method and we have a brief video here to show you this new Surefold system.

[Video is shown.]

The packaged lens is delivered sterile to the operating room table. As you see, it arrives in a vial.

The vial is opened, and the holder/folder system is removed from the vial.

There is a safety cap that is removed. That exposes the H60M lens, which is held between the two prongs. These are then squeezed together, it folds the lens on the correct axis -- again, you see the folding action.

At that time, the lens is then grasped with the insertion forceps of the surgeon's choice.

The Ultem holder was used exclusively in the core study, the 387 patients on here. The Surefold system, however, was validated in a 100-patient clinical evaluation, the data of which is included in your PMA. Again, this demonstrates the folding axis for the H60M lens. Thank you.

DR. KOCH: Thank you. My name is Doug Koch. I am a paid consultant of Bausch and Lomb, and rather glad it is a new day.

I am going to share with you results of the clinical studies of this lens. This is a core study, a single arm, historical control, open label study.

The primary evaluation parameters were best corrected visual acuity and, of course, adverse events.

The accountability at one year complies with the FDA requirement. If you exclude the deceased patients, we had 97 percent accountability. If you include them, the

accountability was 94.8 percent.

The mean age of this cohort was 74.3 years, with a range of 49 to 94.

Getting to the results, the best corrected visual acuity of all cases, of 20/40 or better, was 96.4 percent, well in excess of the Stark grid value of 88 percent, and conversely, of course, worse than 20/40, 3.6 percent compared to the 12 percent on the Stark Grid control.

For best cases, the best corrected visual acuity was 98.9 percent, compared to 94 percent on the Stark Grid. Again, 1.1 percent of the patients were worse than 20/40, compared to 6 percent for the Stark Grid control.

If we look at the distribution of best corrected visual acuity, you can see that 52.6 percent of patients were 20/20 or better, and obviously, the large majority of them up to 20/30, a few of them to 20/40, and then that small percent that were worse than 20/40.

Cumulative adverse events were all below the Stark Grid rates. There was one hyphema, .3 percent, 10 percent of macular edema which is 2.6 percent, but that was actually in seven subjects, which would give you a lower percentage. There was one surgical intervention for iris prolapse.

Persistent adverse events, likewise, were well below the Stark Grid rates. There was actually only one

event present at one year, one patient that was characterized as having mild iritis in a subsequent visit, and the vision was 20/20 throughout.

The Surefold study was designed to validate this new packaging and folding system that Dr. Green described to you.

One hundred and one patients were enrolled. They were implanted with the H60M lens, and this is a core study protocol, with one-year follow up.

if we combine now and look at these tow studies with regard to the issue of broken haptics, which was discussed in the medical reviewers review of this PMA, there was a 1.6 percentage incidence combined, of both core and Surefold studies, of broken haptics.

However, all of these took place in the core study, and that represented eight lenses that had broken haptics.

These generally occurred in the implantation schedule, and actually four of the eight breakages were from one investigator. He broke two lenses on his fifth cases, broke one also at case 15 and case 18 or so.

The remaining four were from different investigators, and those four investigators, they were broken within the first 10 cases of implantation.

Three of the eight breakages occurred when they attempted to fold the IOL along the 3:00 o'clock to 9:00 o'clock method, which you have already heard, is not the appropriate method for folding the lens.

Four of these were observed prior to insertion, and insertion was not attempted. Four were observed after insertion and the lenses were removed.

All the lenses with broken haptics were replaced at the time of surgery. All these patients did well. You don't want to have expectations, but all of these patients did very well.

Optic tears occurred in one percent combined, in the core and Surefold studies. Again, they were exclusively in the core group. That represented five lenses. Again, uniformly, these occurred early in the implantation schedule, with eight implants or less. So, there are four investigators with five optic tears.

Two were observed prior to insertion and insertion was not attempted. Three were observed after insertion and they were replaced at the time of surgery. All patients were implanted with H60M lenses. All patients, again, did well.

Post-market history of this lens, although obviously the data aren't as strict as we would have with a

PMA or a core group, there have been nearly half a million lenses sold since 1995 outside the United States, approximately one third or so with the Ultem holder, and the majority of these with the Surefold system that Dr. Green showed you in the video.

The incidence here of broken haptics is .08 percent. If you look with the Ultem holder, it is .13 percent and with the Surefold .04 percent, and there have been no reports of optic tears.

A PCO, or posterior capsular opacification substudy was initiated in August 1996 at FDA's request. The purpose of this study was to compare the rates of posterior capsular haze and posterior capsulotomy between three lens groups.

Three patients were enrolled and randomized, 100 each into the three lens groups. There were six investigators and results were evaluated at one year.

Again, these are randomized. Obviously, they couldn't be masked immediately post-operatively because the surgeons can readily identify these lens models in a patient's eyes.

There was a one-piece PMMA lens with a 6 millimeter optic and a 12.75 millimeter overall length. There was the H60M, and there was a silicone three-piece

lens with a 6 millimeter optic, polyprophylene haptics.

The primary evaluation parameters were best corrected visual acuity, posterior capsular haze, incidence and grade, posterior capsulotomy incidence.

The posterior capsulotomies were performed at the investigator's discretion. This was conducted according to the standard of practice by these practitioners, and that is why this provision was put in place, rather than have this be dictated by the sponsor.

The best corrected visual acuity was, at one year, comparable in all groups. If we look at the haze rates, you can see that the haze rates -- this is any kind of capsular haze at one year, and would include patients that have already undergone capsulotomy. You can see that the Hydroview fell between silicone and PMMA. This shows it again. Here is PMMA, here is Hydroview, and here is the silicone lens.

There was a statistically significant difference between PMMA and silicone. However, the differences between the Hydroview and the silicone or the PMMA lens were not statistically significant.

Capsulotomy rates are shown for you here. You can see that Hydroview is slightly less than PMMA. The silicone had a lower rate.

Again, it is shown for you graphically, PMMA, Hydroview and the silicone lens.

There was no significant difference between Hydroview and PMMA. There was a significant difference between the silicone lens and both Hydroview and PMMA.

The conclusions from the substudy, therefore, are that the incidence of posterior capsular haze for Hydroview is not significantly different than either PMMA or silicone.

The incidence of posterior capsulotomy for Hydroview was not significantly different from PMMA.

With regard to incision size, the labeling request is that the Hydroview lens can be implanted through a 3.4 to 3.8 millimeter incision.

The investigators in the core study were not asked to implant the lens in the smallest incision possible. However, 123 lenses were reported to have been implanted by the investigators in incisions that were 3.8 millimeters or smaller, hence, the request for this labeling issue.

In conclusion, we believe that these data demonstrate that the H60M is safe and effective. It has an outstanding acuity and safety profile. Because of its unique, one-piece design, with a hydrogel-type optic, PMMA haptics, and yet the construction of a one-piece lens, we believe that it offers a unique alternative to each of these

other products. Thank you.

DR. MC CULLEY: Thank you. And you are available now for fielding questions?

DR. KOCH: That is correct.

DR. MC CULLEY: Panel questions for sponsor. Dr. Pulido?

DR. PULIDO: I guess the biggest concern, obviously, is this broken haptic concern. I think it was a wonderful presentation; the statistics are impressive.

Just some points of clarification. The difference between the P422UV and the H60M is a thinner lens for the H60M over the P422UV?

DR. GREEN: The previous model, the P422UV was a longer overall length and the haptics were somewhat stiffer. This has a shorter length and they are softer haptics.

DR. PULIDO: Because the P422UV had a 6.4 percent broken haptic rate versus a 1.6 percent for the H60M; correct?

DR. GREEN: I am not sure of the broken haptic rate. It sounds like it could be reasonable there. I don't have that data in front of me.

This lens was redesigned actually to accommodate a softer, better profile. The stiffer, longer profile was not desired.

DR. PULIDO: Was it to try to answer this concern?

DR. GREEN: Yes.

DR. PULIDO: The junction -- did the haptic break occur at the junction where the composite occurs? That would seem to be the place of greatest weakness.

DR. GREEN: Actually, that is not the case. These haptic breaks do not break from the junction of the haptic and the optic.

They break at the same place that a single piece haptic would break, which would be just as the haptic starts to widen or thin down, the little area we call the crotch area in there. I can show you a picture here.

DR. KOCH: That is an intrinsic point of weakness in any one-piece haptic. The junction is strong, but that point where it thins out, because of the fulcrum effect, there is a weak point.

DR. PULIDO: Thank you for that clarification. My next concern in that regard was, I believe, from figure 2 or figure 4; I am sorry, I just don't remember off the top of my head.

There was an accompanying table of the tensile strength of the optic. It was chapter 2, the tensile strength was -- page 21, chapter 3. You have the tensile strength of the optic.

My question is, do you have the tensile strength -- if you were to try to take it on its longitudinal axis, where the optic meets the PMMA, and compare that with existing lenses, existing PMMAs, IOLs, or existing other lenses that are out there?

DR. GREEN: Two different points to make here. Number one, when you do pull on the haptic and option junction, as you just mentioned, this more than meets the requirement of a haptic-to-optic bond of, I believe it is 25 grams.

However, if you then change and say, let's analyze exactly where this strength is, and you pull these materials, the break is generally in the optic itself, and not at the junction. The junction is very strong.

As a matter of fact, to your previous point on the broken haptics, I believe there was only one case in the original P422 where there was the question of the haptic/optic junction. There have been no reported breaks ever at that junction past that time.

DR. PULIDO: Thank you.

DR. VAN METER: A question about aging of the lenses. In the past, with the old PMMA lenses, I believe they used to be aged with intensive irradiation of ultraviolet. These were done by heat.

Can you explain if those are equivalent, or justify the aging tests that you did?

DR. GREEN: There were several types of aging studies that were done. There is a standard UV aging test that is in the ANSI and ISO standards. This test, which simulates 15 years in vivo, was done.

However, this is a material test and it really looks at material degradation and biocompatability and toxicology properties. It is not a test that has been designed to look at the optic power.

We have other studies, which are both shelf life studies, which are performed at 45-degree accelerated temperature, as well as studies we have done at up to 80 degrees C, where we have looked at the optic power, and we have not noticed any change in optic power in those studies.

DR. VAN METER: Okay, thank you. On page 12 of the original PMMA submission, it says that the H60M is indicated for primary implantation for correction of aphakia in patients 60 years of age or older.

Then, on page 37, there are 10 patients that were under 60 in your core study. In fact, one patient is under 50.

DR. GREEN: This is always a problem with IOL studies. I think every PMA I have looked at, investigators

enroll patients under age 60, despite the fact that that is not the case.

In fact, if you look at the Stark Grid, the 1993 paper, table 5, there are a whole bunch of patients under age 60, even in the original Stark Grid paper. So, patients got enrolled under age 60, despite the fact that wasn't a requirement.

DR. VAN METER: Thank you. The holders that were used, starting, I guess, with the Burato holder, the Surefold holder certainly seems to work better, but the Surefold holder was only used in a subset of the core patients.

Can you justify the approvability -- any approvability -- of this lens from this data, using the Surefold holder? In other words, we don't have anything other than the subset of patients with the Surefold holder.

DR. GREEN: Well, you have got 100 lenses that were implanted without any optic or haptic breakages.

DR. VAN METER: Is that what is used in your other 500,000 lenses that have been sold worldwide?

DR. KOCH: About 35 percent of those have been the other, the Ultem, and then the remainder have been the Surefold.

The Ultem is still being used some

internationally, and you can see that the incidence of the haptic breakages now is very, very low, even with that Ultem.

DR. VAN METER: Thank you. Last question, concerning the incision size, you have asked for a recommendation of 3.4 to 3.8 millimeters.

Only, by your figures, 31.9 percent were used with an incision size smaller than 3.8, actually, 1.9 were below 3.4.

I am aware of at least one study that has shown that it is pretty hard to implant a 6 millimeter lens that is much smaller than 3.8 or 3.9.

In fact, if you cut the incision smaller than that and insert a folded lens through the incision, and measure it afterwards, it has often expanded to 3.9 or 4.0 millimeters anyway, regardless of the size the initial incision was cut.

Did anyone make an attempt to measure incision size after the lens was implanted?

DR. KOCH: I think in this study investigators measured the incision size before implantation. You are correct; there was not measurement.

DR. VAN METER: Thank you.

DR. KOCH: The only comment I might add to that is

we had done -- not funded by Bausch and Lomb -- a study that has been published in Ophthalmology -- in cadaver eyes, looking at incision size with various foldable IOLs.

The incision size for this lens after implantation in the cadaver eye was 3.5, and that was measured very carefully, with a 6 millimeter optic and a 21 diopter power.

DR. SUGAR: There is a report in this month's Archives of Ophthalmology of the proliferation of lens epithelial cells. This is from David Spalton in London, on the surface of the implants.

I don't see that mentioned anywhere in here. Could you comment on that?

DR. KOCH: Eight investigators reported that lens epithelial cells grew on the surface of the IOL. None of them reported that they caused any clinical issues, and 78 patients had 20/25 vision or better. One patient had macular degeneration.

We are aware of that paper. It is an interesting paper. He actually claims that the lens might be too biocompatible.

On the other hand, it was interesting in that paper that he reported there were actually fewer cellular deposits on the lens of an inflammatory sort. I think there was a positive in that paper, too.

DR. SUGAR: Thank you.

DR. MACSAI: The lens is packed in fluid. Could you tell us what the fluid is?

DR. KOCH: It is distilled water.

DR. MACSAI: It is distilled water?

DR. KOCH: Yes.

DR. MACSAI: Is it recommended that the lens be rinsed prior to insertion?

DR. GREEN: I believe it is. I don't have the labeling in front of me right now, but I believe it is recommended to rinse.

DR. MACSAI: Because distilled water is not compatible with the anterior chamber.

DR. GREEN: Yes, I know.

DR. MACSAI: Are there any recommendations regarding shipping, and have there been any problems with freezing or heating of the fluid with shipping? Does it have to be kept at a certain temperature?

DR. GREEN: We recommend that this lens not be frozen. We have done studies, obviously, on shipping. The problem with freezing turns out to be not a problem with the lens itself. It is actually a problem with the vial, that when you freeze water in the vial, the vial will break.

But the studies we have done have shown that

freezing does not affect the lens optic at all.

DR. KOCH: We checked the labeling. We do recommend thoroughly rinse lens with BSS solution.

DR. MACSAI: Have there been any problems in these half million implanted lenses elsewhere, with discoloration, absorption of pigment, absorption of medications by the lens?

DR. GREEN: I am unaware of any problems in that area. I am unaware of any reports of discoloration or absorption of drugs or any of the like.

DR. MACSAI: If the overall length is 12.5 millimeters, in any of these study eyes or the international eyes, was there ever problem with decentration that required explanation?

DR. KOCH: No, in fact the decentration data we have are excellent.

DR. MACSAI: I know in your study, but I meant in the other half million.

DR. KOCH: No, I am not aware.

DR. MACSAI: Were any of them implanted in the sulcus?

DR. KOCH: In the study there was one implanted in the sulcus. I am sure internationally a large number have been, but just the one in the study.

DR. MACSAI: Have any of those been looked at? Is that okay? What happens in those patients where it is implanted in the sulcus?

DR. KOCH: I have no data on any of that, no.

DR. MACSAI: From the international?

DR. KOCH: No. I have never heard any problems with that. We have never had a lens that has been bag sulcus or sulcus/sulcus.

DR. MC CULLEY: I am sure we have. Internationally, there have been tons of them, but no reports. I would think sulcus would be fine because of the nice rigid construction and the 12.5.

DR. MACSAI: It is the right length for the sulcus.

DR. MC CULLEY: But bag sulcus, you don't have any experience whatsoever?

DR. KOCH: Well, that didn't occur in the U.S. study and we haven't gotten any reports, that I am aware of, about problems from that.

Any time it is bad sulcus, you are always setting yourself up for decentration, regardless of the lens.

DR. MC CULLEY: Right. I was just wondering if this one was accentuated or no.

DR. KOCH: No reports of that. I don't know;

can't answer that.

DR. HIGGINBOTHAM: Any pitting of the lens when the eye capsulotomy is performed, reported?

DR. KOCH: Not reported. My clinical experience is that it yags very easily.

DR. MC CULLEY: Have you hit the lens with the yag to see how the lens response to yag hits?

DR. KOCH: In the IDE studies for the preparation of this lens, we purposefully do studies comparing the pitting behavior of this material compared to other lenses. It was no worse than anything else in those studies. Clinically, I have no other information.

DR. MATOBA: In the core study, I think there were two or three patients who had pitting of the intraocular lens after yag, and they said, in all cases, the visual acuity was better than 20/40 and there were no visual symptoms.

DR. MC CULLEY: So, there were pits in the core?

DR. MATOBA: Yes, I think of two patients.

DR. MC CULLEY: And no description of problems with the pits or unusual pitting characteristics?

DR. MATOBA: One or two pits and they said no visual symptoms, and visual acuity was better than 20/40.

DR. SUGAR: Dr. Koch, can you comment on just how

it unfolds, how rapidly it unfolds, and how easily the trailing haptic is placed.

DR. KOCH: The unfolding is actually one of the nice features of the lens. It unfolds very slowly in the eye, and yet it is not too slow. In other words, it unfolds in a very kind of controlled fashion without, on the one hand, springing open or, on the other hand, your having to sit there having to pry the lens open.

It is a very controlled unfolding, and then the sphere haptic is usually placed with the forceps, although you can dial the lens in as well.

DR. GRIMMETT: Probably an obvious point, but in the international experience, with the low incidence of problems with breaks or tears, under-reporting is, I suppose, a possibility. Was the reporting monitored, if at all?

DR. WALKER: The reporting that we get is a part of our post-market surveillance complaint handling system. For broken haptics and optic tears, it is highly likely that they would return those lenses to us, because they would get them replaced. Then there would be a replacement lens given to them.

DR. MATOBA: In regard to the labeling, are you going to continue to recommend the Oshem Cyber and the

Bausch and Lomb folder as alternative holders for the lens, or are you going to strongly suggest that the physician use only the Surefold?

DR. WALKER: The Surefold is only a folding system; it is not an insertion system.

The labeling submitted with the PMA does include the Surefold labeling system, as well as the two folders that were included in the studies. We include those in there.

There are other folders that it is acceptable to use these with, but those are not folders that we have done the validation, that we feel we want to put in the labeling yet.

DR. VAN METER: My impression is that the lens comes with the Surefold apparatus. You get it with the Surefold anyway.

DR. WALKER: Yes.

DR. MATOBA: In regard to the wound length, some of the patients had wound lengths as long as six millimeters. Do you have some information on that? Was that merely to explant an intraocular lens, or were the wounds made to be that length because of some difficulty with insertion?

DR. KOCH: We did not get reports of difficulty

with insertion. I presume it is related to that. I don't have an answer for that.

I presume it is to take the lens out in one piece, or some people might have put initial lenses in without folding them.

DR. WANG: I have three quick questions. You cited in your study 1.6 percent haptic breakage rate and 1.0 percent optic tear rate and 1.43 percent intraocular device explant rate. I know the international rate is lower.

The important question, I think, is what is the reference rate of other existing intraocular lenses in the market? Are they on the order of 1.0 percent change rate also?

DR. MC CULLEY: Let me break here just a moment. Dr. Rosenthal, is that an allowable question? I don't believe that -- those kinds of comparisons --

DR. WANG: Do we have any guidelines?

DR. MC CULLEY: I don't think -- is there anything in the grid? There is nothing in the grid on that. I mean, this is kind of a gray area, as to whether this is an appropriate question or not.

I am not certain, because I am not trying to squelch it yet.

DR. ROSENTHAL: Not appropriate.

DR. MC CULLEY: Not appropriate; okay.

DR. WANG: I am trying to get a sense. These reported 1-point-something.

DR. MC CULLEY: I think if you knew data that you could quote, you could quote that data. I don't think we can ask them to do that.

DR. ROSENTHAL: I think later on in the discussion, as a point of order, probably you could ask other panel members if they have data in that regard.

DR. WANG: My second question is, there is lens breakage when folded in the 3:00 to 9:00 position, and you also cited 10 degrees off the vertical meridian is the preferred folding meridian.

Do you have any sense of how much degree deviation that the lens breakage tends to occur; let's say, 30 degrees off, that is something you can recommend to the user?

DR. KOCH: No, we really don't have the data about the number of degrees. Basically, we know that you don't want to fold it 3:00/9:00, and you don't want to, when you are doing your folding, encroach upon the haptic/optic junction, but that is the extent of that we have.

DR. WANG: My third question is, there is a claim of UV absorbing. I think the question is related to labeling and that impact of the public in the perception of

this lens.

Is there any data about the percentage of UV absorbing, not only UV but also UVA and UVB, which is also as harmful?

DR. GREEN: Yes, in the labeling, we do give the UV absorption curve for this lens. I believe it is 10 percent, UV cut-off is 380, 10 percent UV cut-off is 380.

DR. JURKUS: I understand you recommend a three-minute insertion time, that the lens would dehydrate after three minutes out of the vial.

Can you tell me, have there been any studies no the rehydration rate. If it takes longer than three minutes to get it folded and put in, does the lens have to be rehydrated?

DR. GREEN: Yes, the lens should be rehydrated. We haven't specifically studied how many minutes of rehydration.

It has been our experience that a short time, like a minute, is sufficient, but we do recommend that it be kept wet as much as possible.

DR. VAN METER: I have a question for Dr. Koch. If this lens, for one reason or another, comes out of the Surefold apparatus, if one picks it up and folds it 3:00 to 9:00, and tries to implant it with the loops crossed,

through a small incision, do the loops automatically tear or can you put it in that way?

DR. KOCH: If you had a large enough wound, you could put it in that way. There have been lenses implanted with a 3:00 to 9:00 o'clock folding. The problem is trying to get the PMMA haptics, since they are both going through the wound at the same time, there is more torque and tension on them, and that is when they are more likely to break.

DR. MACSAI: This is for the staff in the OR. When you remove that little thing, I don't know what you called it.

DR. KOCH: Little safety cap.

DR. MACSAI: Safety cap, do the lenses ever go flying? I mean, do we have to worry about that? How secure are they in this little Surefold gizmo?

DR. MC CULLEY: Scientific terminology here.

DR. GREEN: In that little gizmo, they are actually very secure. The lens could be held in without that safety cap. That is just an extra safety especially for shipping, and who knows what plane it gets dropped off of.

DR. MC CULLEY: So, the gizmo is secure under the thingie.

DR. GREEN: You got it.

DR. MACSAI: If the lens falls off the folder for some reason, it is dislocated from the folder, is there a groove system or something, that the surgical technician could place it back in the folder and still use it?

DR. KOCH: You could place it back in the folder, or you could just fold it with a regular folder.

DR. MACSAI: A folding forceps?

DR. KOCH: Yes.

DR. MC CULLEY: I have a question about the lens. If it is in the eye and the haptic is broken or it is torn, in terms of removal, how easy or difficult is it to remove the lens from the anterior chamber?

Does one need to refold it, cut it, extend the wound? Is it malleable enough that it can simply be pulled back through? How easy, traumatic is it?

DR. KOCH: That is a good question. I don't know that I have the answer to that. I think you could probably fold it in the eye, since it unfolds fairly predictably and actually more rapidly than some of the other lenses that are available.

I think you could probably fold it and you probably could cut it as well. I think the lenses in this study, I think, were removed just by enlarging the wound.

DR. GREEN: I think one of those was removed by

cutting, but most of them were enlarged, as I recall. It should be able to be cut fairly easily.

DR. MC CULLEY: Any more questions?

One of these days, is the FDA going to deal with the 60-year-old thing? I think if we polled the public, or the practicing ophthalmic community, I wonder how many know that there is no lens labeled for less than 60 years of age.

DR. ROSENTHAL: We are currently attempting to address this problem.

DR. MC CULLEY: Other questions for sponsor?

We will excuse the sponsor at this point and ask the FDA to come to the podium and table for their presentation.

I want to thank the sponsor for a well-presented PMA, and responsiveness to questions.

Dr. Van Meter, don't forget you are our scribe for questions, concerns, that we rely upon you for completeness and articulation. Don't let Miriam distract you. Behave.

DR. BOULWARE: Good morning. I would just like to introduce PMA P990014 for the Hydroview IOL.

My only statement is that I would like to thank the review team for all of their hard work, and timely reviews, in preparing this document for panel review.

At this time, I would like to introduce Susanna

Jones, who is a branch toxicologist, and the team leader for this document.

MS. JONES: I am Susanna Jones. I am the team leader for PMA P990014.

I would like to thank the sponsor for providing us with an advance copy of their presentation, so that we could avoid unnecessary duplication of details.

The following individuals were part of the FDA review team. Dr. Berman is the clinical reviewer. Claudine Krosik did engineering, Susan Gouge, microbiology, Chang Lao, statistics, and I was the toxicology reviewer.

After reviewing the PMA, there remain some minor engineering and clinical issues that have to be resolved before the final approval of the PMA. However, the PMA was deemed ready for panel reviewers.

The primary panel reviewers are Drs. Alice Matoba and Woodford Van Meter.

FDA determined that a panel review of the PMA was appropriate for the following reasons. One is that the chemical composition of the optic material is different from other PMA approved materials.

Also, a panel review of the potential safety issues regarding optic tears, haptic breakage, intraoperative explants and claims about incision size was

deemed appropriate.

Dr. Berman will now summarize the clinical issues.

DR. BERMAN: Good morning, everybody. I would like to thank the sponsor for their very complete presentation, and I have also read both of the primary panel reviews, which are also very complete.

I don't think there is any additional information that I need to present at this time. So, I would like to go ahead and pose the questions for panel consideration.

Question number one. The PMA study results demonstrate a 1.6 percent incidence of haptic breakage, 1.0 percent incidence of optic tears and 1.43 percent incidence of intraoperative device explant.

Do these data demonstrate a reasonable level of safety. Are there any additional safety concerns? Does the panel feel that precautionary wording in the labeling is sufficient.

Question two. The sponsor makes a claim about incision side, that the folded lens can be inserted through an incision of 3.4 to 3.8 millimeters.

However, PMA data demonstrate a mean incision length of 3.9 millimeters. Only 29.9 percent of eyes fell within the proposed range and 1.9 percent fell below the range.

Does the panel feel that this labeling claim is supported by the PMA. Should the claim be modified.

Question three. Does the panel recommend that anything be added to the labeling that is not currently present?

Question four. Does the PMA data provide reasonable assurance of safety and efficacy to support approval of the Hydroview foldable, posterior chamber IOL?

DR. MC CULLEY: Does that conclude your presentation?

DR. BERMAN: Yes.

DR. MC CULLEY: Thank you for not reiterating already well-presented data. Does the panel have any questions for the FDA?

DR. PULIDO: I think, Dr. Berman, this was a very good review that you gave us. I just had some questions. Why did you want them to have to tell us where the incision locations were, and whether they were all phakoemulsifications.

How did that change what they were submitting to us, and the data that we had to present. I just want to make sure that our sponsors don't have to present more extraneous information than is necessary for us to make some decisions.

DR. BERMAN: We ask these questions of all IOLs, and it is for a number of reasons. First of all, it is to make sure that the cases presented represent a typical practice of cataract surgery across the country, and that they are implanted in a sufficient distribution similar to how they are going to be implanted when they get out to be marketed.

DR. BOULWARE: Could I comment? When we discussed the previous draft of our IOL guidance document, incision location and size were actually two of the items that the panel recommended be collected in IOL studies.

DR. WANG: Does FDA have any guidelines regarding this tear and breakage rate?

DR. BOULWARE: No, we don't at this time.

DR. MC CULLEY: If I understand the issues here, there are two issues and they are intertwined. It is incision size and breakage.

It seems that, if I understood sponsor, that the incision size, or the time of breakage -- folding is critical, but the time of breakage otherwise is tied to insertion through the wound, which is tied to incision size.

If you try to make it smaller, you are going to have greater breakage. From an FDA standpoint, does that ring true or not? FDA is not sure. Well, it will come out

in our discussion.

DR. BERMAN: I think the sponsor may be able to address that. I think that they may be related. I am not sure that they are completely related.

DR. MC CULLEY: You are putting a fragile object through a space. This is just intuition, and some clinical experience.

DR. BERMAN: I agree with that, but I think that some of the tears and breaks have to do with the way the lens is folded, nothing to do with how it is inserted.

DR. MC CULLEY: Right, and I said that, folding aside. It looked like half of their breaks in the data they presented were related to folding, prior to, or manipulation before going in the eye. Roughly the other half were in the eye.

I am making an assumption, which is always risk, that the majority of those that did not relate to manipulation before insertion, but they occurred as insertion occurred.

Again, we are supposed to bring our experience to the room. From just my clinical experience, putting it through the wound is the riskiest time for haptic and optic, relative to their integrity.

DR. BERMAN: I would like the sponsor to address

that further, but from my own recollection, I know that some of the lenses were reported by the investigators to have been broken after the time of actually insertion through the wound, when they were manipulated inside the eye.

DR. MC CULLEY: We have two primary reviewers. Do we have any other questions for FDA? Okay, let's go on to the first primary review, Dr. Van Meter.

DR. VAN METER: I appreciate the sponsor supplying a complete account of the data in the study, and the comments of Susanna Jones and Sheryl Berman, which were helpful.

I will not repeat the data, which has been available to everyone. To touch the high points, accountability was satisfactory, with effectively 95 percent accountability, excluding patients who had died.

Of the 11 patients lost to follow up, nine of those patients had 20/25 vision at last examination and no reason to think that the lens does not perform well.

I think the efficacy of the lens has been well established and the safety issues are not really a concern to me because the incidence of broken haptics, which was 1.6 percent, and optic tears of 1.0 percent, appeared to be related to learning curve.

It is unusual that we have a sponsor's

presentation here with over 400,000 lenses implanted worldwide. I think it is hard not to look at some of that experience.

Worldwide, the incidence of broken haptics is 0.16 percent and optic tears of 0.06 percent, which I think are quite acceptable.

I think labeling can address the learning curve, and I will discuss that in my conclusions.

There were four eyes that had surgical complications, one with a decimase detachment, one an anterior chamber hemorrhage, one with iris damage and one an anterior capsular tear. All four of these eyes did well, even though the protocol states that surgical complications such as these, which happened before the lens was implanted, were actually contraindications to Hydroview use. However, the lens was put in anyway, and the patients seemed to do well.

Best spectacle corrected acuity showed 20/40 vision in 96.4 percent of patients, exceeding the Stark Grid.

Now, I have four concerns before we get to final recommendations. The variability in folders is, I think, justifiable and understandable now.

It would be nice if it didn't make any difference

what folder was used, but the Surefold apparatus, as we have seen demonstrated here, seems to be superior, and a step ahead of having manual folding done by a variety of folders in a variety of operating rooms.

I think because the Surefold inserter was not used in the PMA patients, that it should be noted in labeling that the effectiveness of the Surefold is based on a subset of the core patients.

This intraocular lens is clearly more sensitive to improper handling than PMMA lenses, and other lenses on the market, and the risk of haptic breakage and optic tears, which are related to forceps manipulation of the lens and implantation, leads me to believe that a fairly detailed recommendation for implantation would be helpful.

I don't think you can specify exactly how the lens should be implanted, but I would note, for instance, that the risk of folding lenses higher than, say, 27 diopters leads to an increased risk of lens damage, and folding the lens off axis, which a number of other foldable lenses are, indeed, folded on a different axis than 12:00 to 6:00.

If this lens, for one reason or another, falls off an inserter, it would be nice if a surgeon could pick it up and put it in in different ways.

I think you need to be clear in labeling that one

does so at one's own risk.

An anterior capsular bag probably needs to be required for implantation of this lens. Theoretically, I believe the lens can be placed in the sulcus in front of a torn anterior or posterior capsule, using capsular flaps as a guide.

Unfortunately, sometimes a radial anterior capsular tear occurs after the lens has been implanted in the eye and as the lens unfolds, and sometimes you can't always tell this.

I think the determination of putting the lens in only with an intact anterior capsular flap, which I got the impression from labeling is required, might be a suggestion rather than a requirement.

I believe the lens would do well if the anterior capsular tear is controllable, and because you can't always tell there is a capsular anterior tear at the time of implantation.

In conclusion, I believe that this PMA provides sufficient information on safety and efficacy to support approvability.

My concerns about the safety and fragility of the lens can be sufficient covered in labeling, and I would specify the labeling include the risk of haptic breakage,

tears, a notation that most of the tears occurred with folding or implantation, including the risk of folding thicker lenses, for example, thicker than 27 diopters.

I believe that the labeling claim about incision size is not supported by the data, because clearly, the incision sizes in this study, ranging from smaller than 3.4 to 6 millimeters actually reflect the practice of medicine and what I believe surgeons do in general. I would leave incision size out of this. Thank you.

DR. MATOBA: I will try not to be too redundant, but I will repeat one or two things that have been already mentioned.

This was a single armed, historical controlled, open label study to evaluate the Model H60M Hydrogel PMMA lens.

In terms of accountability, 387 patients were enrolled in the core study, and at form 5, which was the end point at one year, 332 patients were available, and this is an accountability level of 85.8 percent.

Fifty-six patients were missing and, of those, an additional 27 were said to have been seen at a later visit, bringing the total up to 359, or 92.5 percent accountability.

However, most of the data that was presented in

the document was based actually on the 332 patients, or 85 percent accountability.

In terms of efficacy, the primary parameter was best corrected visual acuity at one year, or form 5, and the Stark Grid of 88 percent was exceeded, in that the patients achieved best corrected visual acuity of 20/40 or better at a rate of 96.4 percent, and that is for an N of 332.

For best case, as Dr. Koch stated, the Stark Grid is 94 percent and the study achieved 98.9 percent.

In terms of both cumulative and persistent adverse events, for all categories, the study achieved or exceeded the Stark Grid.

Actually, of the 10 patients noted to have either accumulative or persistent adverse events, of those 10 patients, seven out of 10 achieved visual acuity or 20/40 or better at one year.

So, overall, the safety and efficacy issues were not a major problem. However, there is a concern regarding the incidence of haptic breaks and optic tears, haptic breaks at 1.6 percent, optic tears at 1.0 percent.

I think this is higher than most PMAs that are currently being utilized. Unfortunately, I hear that the FDA has not set a level or standard that should be met.

In terms of the sponsor's statement that over

400,000 Hydroview lenses have been sold internationally and the reported incidence of broken haptics is only .06 percent, I agree with Dr. Grimmett, that the monitoring system is not clearly -- it is not clearly how effective a monitoring system may be in place, and there may be a significant under-reporting of the incidence of optic tears and haptic breaks.

The Surefold system appears to be a significant improvement over the folding system that was utilized in the study with 101 or 100 patients having been studied with a zero incidence of breaks and tears.

However, when you are looking at a complication with an incidence of between 1.0 and 1.6 percent, I think 100 is not an adequate number to prove that you have significantly decreased that complication rate.

I would actually like to see more patients studied, just for the effect of Surefold on the incidence of haptic breaks.

Also, although the statement was made that the incidence of breaks maybe just reflects a learning curve, data was not presented to support this claim, that there would be a trend toward smaller numbers of complications with greater experience of the surgeon.

I had no concerns regarding the posterior capsular

pacification. The substudy that was performed did show that the incidence of posterior capsular pacification and capsulotomy were not significantly different for H60M compared to either the P54UV PMMA lens or the silicon SI30MB lens.

In summary, I think that this lens is approvable with appropriate -- well, if we were to receive some additional information regarding the safety of the Surefold system, and with some labeling changes to reflect our concerns.

DR. MC CULLEY: Thank you. Are there questions for the primary reviewers at this point, to clarify their presentations?

DR. HIGGINBOTHAM: Dr. Van Meter, you mentioned that wound size shouldn't be an issue. Would you suggest at least a minimum wound size or would you just leave it up to the practice of medicine?

DR. VAN METER: I would leave it up to the implanting physician. The reason I don't think a minimum wound size is appropriate is, a certain size -- Dr. Koch suggested that they had used cadaver eyes to say that the lens could be implanted through a 3.5 millimeter incision measured afterwards.

I think the elasticity of live eyes is probably

different, but you know, my concern is that, no matter what the minimum wound size is, you could probably put the lens through a one millimeter incision, although by the time you got it in, it would have stretched to four.

For this reason, I think that it is a practice of medicine issue. I think that implanting surgeons know what size wound they make, and I am quite certain that that information is not necessary to the efficacy of this lens. I would leave incision size out of the picture.

DR. MC CULLEY: Let me ask for a point of clarification from the FDA. In other labeling on lenses, is it common or typical, atypical, never, first time, whatever, to state the wound size for a lens as part of the labeling? Is that standard? In that case, we would need to do it.

DR. ROSENTHAL: Again, we prefer you to make your decisions based upon --

DR. MC CULLEY: I am trying to get a real world -- a sentiment has been stated -- let me state it another way. A sentiment has been stated that we not address the issue of wound size in product labeling. Is that consistent with FDA practice now, or does FDA need a statement on wound size?

DR. ROSENTHAL: Apparently we do have statements with minimum wound size. It is not required.

DR. MC CULLEY: Not required. Is it preferred by the FDA, or do you not care; you want to leave that to us?

DR. ROSENTHAL: I think we would like to leave that to you.

DR. SUGAR: Is this an appropriate time to discuss that issue?

DR. MC CULLEY: Sure, I think we can go ahead now to panel discussion of the PMA.

DR. SUGAR: I think that, as in other discussions of labeling, we should have the labeling present the data that the sponsor obtained.

That data can be used by the physician as he or she sees fit, but it is worth giving them the information that was used to implant whatever lenses were used in the study, as opposed to having no baseline to know where to start.

DR. MC CULLEY: That certainly puts data out there. I am not sure, if we need to have something there that is really going to be used in practice for guidance of the ophthalmologist who will be implanting, we might have made a requirement for doing that, but I am not sure that we would be providing the ophthalmologist with the guidance, if we feel we need it, that we would be attempting to give to them.

DR. VAN METER: I think that Dr. Sugar is probably going to give us an out. The problem with specifying a wound size is, the data in this study really doesn't give us a wound size because of the wide variation.

There is a problem with specifying a minimum wound size. If we say that 31 percent of patients had implantation of a lens through a wound 3.8 millimeters, that would perhaps give the implanting surgeon the information they need. Is that what you had in mind?

DR. SUGAR: Yes, plus the range.

DR. MC CULLEY: Does that seem reasonable?

DR. HIGGINBOTHAM: I think there should be something, at least a minimum, for those of us who don't do 30 cataracts a day, to have a minimum, or some information. I like Dr. Sugar's suggestion.

DR. MC CULLEY: So, you liked Dr. Sugar's suggestion. So, Dr. Sugar has dealt with this issue well for us. Any more discussion before we go to panel questions?

I would like to call the FDA back to present your questions to panel.

DR. VAN METER: Dr. McCulley, is it possible to ask one question of the sponsor at this point?

DR. MC CULLEY: Sure, we can do that. I would like to recall sponsor to the table.

DR. VAN METER: My impression from the data is that most of the lens loop breaks and tears occurred with folding or implantation.

Are you aware of any case in which the lens was damaged or torn after it was implanted in the eye?

DR. KOCH: One of the eight haptic breakages occurred with one surgeon -- he stated it occurred with the manipulation of the lens in the eye after unfolding. That is the only time that we are aware of, intraoperatively.

DR. VAN METER: We have one anecdotal case, after the lens was put in.

DR. KOCH: Exactly.

DR. SUGAR: I should have asked this earlier, but your lower limit is 15 diopters. Was that a marketing practical decision, or was that an engineering decision, that if you get thinner at the edge than that, you can't fuse the haptic to the optic.

The sequel to that question is, do the lower power lenses have more risk of breakage?

DR. KOCH: No, the decision to stop at 15 diopters had nothing to do with the haptic bonding to the optic. That was not an issue at all.

DR. MC CULLEY: Do you have any association with wound size and incidence of haptic or optic breakage or

tearage?

DR. KOCH: No, we really don't. So many of these occurred with some form of manipulation, not directly at the time of implantation.

DR. MC CULLEY: You are talking about the ones that were associated with implantation?

DR. KOCH: Correct.

DR. MC CULLEY: You have no data or your data does not support an association with wound size?

DR. KOCH: We haven't looked at that.

DR. ROSENTHAL: I just want to point out, it may be anecdotal but it is a case, out of the 300-some, in which this lens broke while it was being manipulated in the anterior chamber.

DR. MC CULLEY: It was a misused word, Dr. Van Meter.

DR. ROSENTHAL: So, if you are implanting 460,000 of them, I mean, the corollary is that a certain percentage of them may break when you are manipulating them in the anterior chamber.

DR. MC CULLEY: But there was one in this study.

DR. ROSENTHAL: One in this study.

DR. MC CULLEY: I would like to note for the sake of panel and audience that sponsor was recalled to the table

at the request of a panel member and the chair granted that request.

DR. FERRIS: I just had a question to follow along the discussion of putting the range of incisions that were used.

That range was quite broad and went down to two or something. Is there some size below which the sponsor really feels you shouldn't try to insert this lens, or is it okay to just put this -- does the sponsor feel that putting that whole range is appropriate? As a retina person, I don't have a clue.

DR. KOCH: I think Dr. McCulley's answer is the right one. Every surgeon kind of knows his or her right incision size, although most surgeons don't measure it. So, we don't really know, and the sponsor doesn't really know what the right size is.

Without post-implantation reporting, it is difficult to know what, as Dr. Van Meter pointed out, what we ended up with.

DR. ROSENTHAL: The issue is one of labeling and what the sponsor wishes to say, and whether or not the panel feels that it is appropriate to say it. If not, is it appropriate to do it another way, and that is what we are asking your recommendation on.

DR. MC CULLEY: Dr. Sugar has the specific here that is requested here, I believe.

DR. ROSENTHAL: Dr. Sugar has already made the comment. I just want to clarify it.

DR. MC CULLEY: What is in -- that is what is in the proposed labeling?

DR. SUGAR: In the submitted labeling it says, an incision size of 3.4 to 3.8 millimeters is required for this technique, depending on the lens power.

I don't know that you really have data other than to say that size was used. It was actually larger than that and your mean, I think, was 3.9.

DR. KOCH: Right, although we did have at least 123 lenses that were implanted in incisions that were stated to be 3.8 or less, which is why we are thinking that it can be implanted, depending on the surgeon's technique.

DR. SUGAR: I ma just suggesting that it doesn't have to say required. You just say what your experience was.

DR. MC CULLEY: This was sufficient on this issue. Any other questions while sponsor is at table? We will excuse you again.

DR. PULIDO: For the record, I would like to state that retina surgeons are not clueless.

DR. GRIMMETT: Just a general comment before Sherry Berman makes her presentation. In follow up to Dr. Macsai's comment about the distilled water, about seven or eight years ago I did an investigation with Dr. Adelhauser, and it was published in the AJO in 1992 or 1993, regarding hypoosmotic insults to the corneal endothelium, both functionally and anatomically, by electron microscopy.

We found, in a in vitro profusion system, that the endothelium is extraordinarily sensitive to hypoosmotic insults, as well as lack of electrolytes.

Just for the record, on page 169 of the labeling in item seven, it does says, thoroughly rinse the lens with BSS solution, which I endorse heartily, based on the data I published.

DR. MC CULLEY: Thank you. I think we really had already dealt with that issue, with sponsor's response. I would like to ask the FDA to come forward and present your questions for panel.

DR. BERMAN: Question number one. Do the data for haptic breakage and optic tears demonstrate a reasonable level of safety. Are there any additional safety concerns, and does the panel feel that precautionary wording in the labeling is sufficient?

DR. MC CULLEY: Dr. Matoba, would you like to start the answer for us?

DR. MATOBA: I do have concerns about the incidence of reported haptic breakage and optic tears, and the incidence of intraoperative device explant, which is partially related to the haptic breakage or optic tears.

I would like to see an additional 100 or so patients with the Surefold system, demonstrating more clearly a decrease in the incidence of breakage.

DR. MC CULLEY: Would you like to clarify or bring FDA reality into that?

DR. ROSENTHAL: I mean, could that be done bench testing? I am not sure what --

DR. MC CULLEY: Given the options available to us, to require anything like that is tremendously difficult within the system.

DR. ROSENTHAL: We have data on half a million. Can you clarify what you want?

DR. MC CULLEY: What we want is assurance of -- the concern is the haptic breakage and the optic tearage. I think we need to possibly, if you could clarify for us in terms of, we want something in the labeling to warn about that.

DR. ROSENTHAL: That is no problem.

DR. MC CULLEY: I understand that. There is a little bit of a sentiment, unless we are going to accept the international experience, which is an option, although it wasn't presented -- it was presented anecdotally, I guess -- are we going to want some kind of reporting post-market.

I know that post-market surveillances per se are somewhat problematic. Is there something in that area that is reasonably done that we could request to give some assurance and comfort level to the panel.

DR. ROSENTHAL: I think you could put in your conditions of approval that the company should provide you with information in their annual, or after six months of experiences, on how many lenses were exchanged for what reasons.

I would imagine, in the United States, if you broke it you would send it back.

DR. MC CULLEY: Yes, these lenses, again, the economic issue here, if a lens has a problem, we send it back so we get replaced and don't buy it. Otherwise, we buy it and eat the cost.

DR. ROSENTHAL: And the company, I presume, keeps a record of all the lenses that are sent back to them. I don't think that is an unreasonable demand.

If you are concerned about the Surefold system,

that it actually works, you could do that as bench testing, you could do hundreds of lenses, to be sure that, when you folded it and somebody took it with a forceps, that it didn't break.

DR. MC CULLEY: We could deal with that in the same manner. We could ask the company to report the experience after six months, 12 months, of the incidence of returned lenses, and provide data on why the lens is returned and the method that is used in folding and inserting.

DR. ROSENTHAL: I am sure that is not an onerous task for the company, although I can't speak for the company. I think it is a reasonable request.

DR. MC CULLEY: The answer, then, to this question would be yes, with Dr. Van Meter having gotten down what we have requested. Then, are there other additions and modifications?

DR. FERRIS: I want to make sure what we are asking. Am I wrong? Have there been hundreds of thousands of these lenses folded with this Surefold thing? The company has probably already provided us with this information, that a tenth of a percent of these are coming back to them.

I am sure that is an underestimate of the total

number that are broken. It can't be an over-estimate. It can only be an under-estimate. They know what their denominator is, and their numerator may be low, but we already have a range, and that is that it is some place between one percent and a tenth of a percent.

The question is, for labeling purposes, and from an individual physician's point of view, we use statistics all the time, but when it is down that low, the difference between one tenth of a percent and one percent, or 001, from an individual's point of view, the chances of an individual lens breaking is very low. That is what the labeling is supposed to say.

I don't think that knowing that number with our precision would help you very much. That is my statistical view of this, that whether it is one percent, a tenth of a percent or a hundredth of a percent.

DR. MC CULLEY: I think we want a gestalt sense, not a statistical sense.

DR. FERRIS: Don't we have a gestalt sense?

DR. MC CULLEY: Well, we do, to a degree. If panel wants additional, I think we can add to the comfort level by requesting what was suggested.

DR. PULIDO: Going with Dr. Rosenthal's idea about bench testing, we have the tensile strength of the optic,

and we know what the tensile strength of the PMMA is. Can one take the combined composite and bend it at that point to see what the tensile strength is of the combined composite at that -- not at the juncture, but rather, at the point of breakage, and compare it with IOLs that have already been approved?

DR. MC CULLEY: My impression is that that would not be an appropriate request. Is that correct, FDA? Did you understand the question?

DR. BOULWARE: The company did a folder validation on the Surefold that includes putting the lenses through the folders and doing an extensive battery of tests after the lens has been folded and held in the folder for a certain amount of time, and then a range of both optical and mechanical tests dimensions are all measured as part of the folding validation.

So, all of that bench testing has already been done and submitted in the PMA.

DR. MC CULLEY: And you assess that for acceptance or adequacy. That is something you do, that doesn't come to panel; correct?

DR. BOULWARE: That is correct.

DR. PULIDO: Then I feel very comfortable with the results.

DR. MC CULLEY: The results, not requesting additional -- okay. Just a straw, results stand with the international assurance in reporting, without the request for additional post-marketing reporting? All in favor of not requesting additional post-marketing reporting, straw vote?

[Hands raised.]

DR. MC CULLEY: All wanting additional reporting?

[One hand raised.]

DR. MC CULLEY: That's good; stick by your guns, but your idea is defeated.

DR. BOULWARE: Could I just add one more thing? This might ease some of Dr. Matoba's concerns. The company is required, in their annual reports, to report on any reports of problems, including the haptic breakage, and especially to report on them if the rate were to exceed what is currently in the labeling. We would see that data on an annual basis.

DR. MC CULLEY: Right, that gives us an added degree of comfort. I don't think we want to see a 1.6 and a 1.0, ideally. Does this answer your first question? It is answered yes. Second question?

DR. BERMAN: The second question regards the claim about, the folded lens can be inserted through an incision

of 3.4 to 3.8 millimeters. Does the panel feel that this labeling claim is supported by the PMA? Should the claim be modified?

DR. MC CULLEY: Dr. Sugar, would you like to suggest what the labeling should actually be?

DR. SUGAR: The present labeling doesn't say, can be. It says required. I don't think they should put a requirement in there.

I think they should state the range of incision sizes in their study, and the mean.

DR. MC CULLEY: Is that agreed?

DR. VAN METER: And that the incision size was not measured following implantation.

DR. MC CULLEY: They stated it was not, that initial or entry size. All right, next question?

DR. ROSENTHAL: Can I just clarify? If they put in a range and 1.9 were put in under the range, then it can, theoretically, be inserted under the range.

DR. MC CULLEY: Yes.

DR. ROSENTHAL: I want to try to protect the company from getting into trouble in the future. Whether they appreciate this or not, I don't know.

As you know, they will want to make claims to make this lens as attractive as possible. If they say it can be

put in an incision 3.0 millimeters, well, you know, it can be put in an incision, but it is probably not advised to be put in the incision.

DR. SUGAR: They could put, 1.9 percent were put in incisions less than 3.4, 29.5 percent were placed in incisions between 3.4 and 3.9 millimeters.

DR. VAN METER: Dr. Rosenthal, we are talking about two different ranges. The company's range is 3.4 to 3.8 with the lower end of 3.4. The range of the incisions put in, in the study, went all the way down to 2.9, and 1.9 percent were put in between 3.4 and 2.9.

The range that we would say, some were put in as low as 2.9, others were put in all the way up to 6.0. It seems to be pretty clean, if we just use the data that they presented to us.

DR. SUGAR: Just put the percentages that were in the different ranges.

DR. MC CULLEY: The risk here is that in our macho world, in this situation, smaller is better.

DR. PULIDO: Macha world.

DR. ROSENTHAL: In our diverse macho world.

DR. MC CULLEY: So, the recommendation is, as Dr. Sugar stated us, as you are going to have to state back to us in a minute, is there further clarification on that

recommendation? Dr. Wang?

DR. WANG: I would like to suggest, just give the range that they have used and give the mean, without going through percentages.

So, this lens can be inserted through an entry wound size of 2.9 to X with a mean of what, 3.9.

DR. MC CULLEY: I think that is really risk. I think that does cause problems. Again, the smaller the wound, the less likely to have to put stitches, the less likely to affect astigmatism and so on and so forth. The tendency is to go small.

My judgement is that if you start pushing toward the small size with this lens, it is when it is going to have more haptic and optic problems.

That, whether the company appreciates this or not, is going to work against the company. If you have a lens in that is torn or a haptic is broken, that surgeon is going to say, gee, do I want to stick this sucker in, because I had to increase my wound significantly. I think it works against them.

I don't think we want to have it where this lens is marketed to be pushed for the super-small wounds. I think that will work against everyone and, in actual fact, work against the company.

DR. WANG: How about, we modify that. The mean is 3.9. They say, 95 percent of lenses in the clinical trial have been put through 3.3 through 4.2. Give what the majority of the surgeons have done with this lens.

DR. MC CULLEY: Was the majority between 3.3 and 4.2?

DR. WANG: The mean is 3.9. I would imagine it is a standard deviation on both sides.

DR. FERRIS: That was my comment. First, my stupid retina question, I think, addressed what you were getting at.

That is, I think the range is a very poor description of the distribution. In fact, it is one of the worst distributions, because outliers become set in stone.

A mean, plus or minus two standard deviations, would be a much better description of the distribution than the range, I think.

DR. MC CULLEY: That makes good sense, I think. Are you going to be able to state that back clearly or do you need someone to tell you?

DR. VAN METER: We mentioned the mean wound size, plus or minus two standard deviations for the labeling.

DR. MC CULLEY: Okay, next question?

DR. BERMAN: Does the panel recommend anything be

added to the labeling that is not currently present?

DR. MC CULLEY: Any additions?

DR. WANG: I would like to make sure that -- there is a claim of UV absorbing and 10 percent does leak through. The cut off is 90 percent being clarified in the labeling. It is not 100 or 99 percent.

UV absorbing in the area of, say, sun glasses, is often 99 percent absorbing. This is only 90 percent.

DR. YAROSS: I would just point out, as I think FDA looks like they are about to also, that is class labeling. That is handled uniformly across the IOL product line, that the 10 percent cut off is what is specified, Dr. Wang.

DR. HIGGINBOTHAM: This is, I guess, probably a class labeling as well. As I look at their labeling considerations, they are suggesting that glaucoma patients, actually, medically uncontrolled glaucoma patients be excluded.

They had at least four patients in the study that had previous glaucoma surgery. They are also stating that you can't do a trebeculectomy with this insertion.

So, I imagine that this language that is included here is probably related to the class, but I would like to maybe offer the suggestion that perhaps we might consider in

the future, in terms of revising class descriptions, that this language might be modified, given the numbers of combined procedures that are being performed in this country.

I think it unnecessarily excludes a whole class of patients.

DR. ROSENTHAL: That is an excellent suggestion, Dr. Higginbotham. I am not intimately knowledgeable about this. It is not standard labeling, apparently.

DR. MC CULLEY: I do have a question, and those of you who reviewed it more thoroughly, was there any issue about drug depoting or depositions in this lens? There must have been.

DR. MACSAI: I asked the sponsors and they said not to their knowledge. I don't know if any studies were done pre-insertion.

DR. HIGGINBOTHAM: Given Dr. Rosenthal's comment, can I offer the suggestion to the group, to consider deleting chronically medically uncontrolled patients with glaucoma, as a contraindication for this lens, and perhaps delete also the addition of glaucoma surgery when inserting this lens, because it is a standard of practice.

DR. ROSENTHAL: Apparently that was the sponsor's decision. Normally, we don't ask them to remove --

DR. MC CULLEY: I would wonder about the risk of drug being deposited or taken up and held in the lens. I would think that that is probably wiser, with this hydrogel lens.

DR. ROSENTHAL: We have no data on depoting of any drugs. It is not required as part of the PMA.

DR. HIGGINBOTHAM: This is a high water content lens.

DR. BERMAN: The water content of this lens is 18 percent.

DR. HIGGINBOTHAM: So, compared to other lenses, is it more or less?

DR. BERMAN: No.

DR. HIGGINBOTHAM: So, water is not going to behave as a depot. I would say it is less likely.

DR. MC CULLEY: I would go back to soft contact lenses and the hydrogels and soft lenses, and drugs can certainly depot in contact lenses, and some adrenochrome pigment, for instance, in contact lenses that are, many of them, similar materials.

Simply, with the contact lenses, you take them out, throw them away and put another one in, or change to something else. It would be tough to do that with this lens.

DR. HIGGINBOTHAM: It is a different location.

DR. MC CULLEY: The concentrations are going to be different. You have got a different environment; I just don't know.

DR. HIGGINBOTHAM: We have a different environment and we haven't seen it with other lenses necessarily.

DR. MC CULLEY: The other lenses don't have this kind of polymer. That is why it was brought to us, is that it is a new, very different kind of polymer.

I would favor that being left in the labeling with the unknown, and with the experience of soft lenses on the surface. Granted, very different, but it is a concern.

DR. HIGGINBOTHAM: There were glaucoma patients in the cohort.

DR. MC CULLEY: They didn't follow them for long periods of time. I don't know what their drugs were. There is probably not enough to answer that issue. That is a concern, and I am sure it is for the company.

So, we have gotten our recommendations there. Next question.

DR. BERMAN: Does the PMA data provide reasonable assurance of safety and efficacy to support approval of the Hydroview Foldable Posterior Chamber IOL.

DR. MC CULLEY: Dr. Van Meter, would you like to

answer that?

DR. VAN METER: Yes.

DR. MC CULLEY: Agreement. At this point, does that answer all the FDA's questions?

DR. BERMAN: Yes.

DR. MC CULLEY: Does the panel have any additional input? I would like to reopen the floor for a potential 30-minute open public hearing, where individuals may come to the podium to state their views.

Each individual will be limited to five minutes presentation, and the period will last no longer than 30 minutes. Is there anyone who wishes to come forward to speak? Seeing none, the open public hearing session is closed.

I would like to invite the FDA now to make its closing comments, if you have any.

I would now like to invite the sponsor to come forward to make your closing comments within a five-minute period.

DR. KOCH: Thank you, Dr. McCulley. We have really very little to add to the discussion. I appreciate the discussion very much.

With regard to hydrogels and absorption, the sponsor did not evaluate that. However, there are,

internationally again, 500,000 lens implanted or so that have not had any reports. There are obviously lots of glaucoma patients.

There are other hydrogel materials, actually, even 38 percent water content hydrogels, with years and years and years of experience in the eye that have not had any reports.

So, we don't think deposition or absorption is a problem, as Dr. Higginbotham suggested, but certainly don't have data to support it.

Otherwise, we appreciate the discussion and thank you for your time.

DR. MC CULLEY: Thank you. We will now ask Ms. Thornton to read the voting options open to the panel.

MS. THORNTON: The medical device amendments to the Federal Food, Drug and Cosmetic Act as amended by the Safe Medical Devices Act of 1990, allows the Food and Drug Administration to obtain a recommendation from an outside expert advisory panel on designated medical device premarket approval applications, or PMAs, that are filed with the agency.

The PMA must stand on its own merits, and the panel's recommendation must be supported by safety and effectiveness data in the application, or by applicable

publicly available information.

Safety is defined in the act as reasonable assurance based on valid scientific evidence that the probable benefits to health under the conditions of intended use outweigh any probable risks.

Effectiveness is defined as reasonable assurance that, in a significant portion of the population, the use of the device, for its intended uses and conditions of use, when labeled, will provide clinically significant results.

The panel's recommendation options for the vote are as follows:

Approval, there are no conditions attached.

Two, approvable with conditions. The panel may recommend that the PMA be found approvable subject to specified conditions, such as physician or patient education, labeling changes, or further analysis of existing data.

Prior to voting, all the conditions are discussed by the panel and listed by the panel chair.

Not approvable. The panel may recommend that the PMA is not approvable if the data do not provide reasonable assurance that the device is safe or, if a reasonable assurance has not been given, that the device is effective under the conditions of use prescribed, recommended or

suggested in the proposed labeling. Thank you.

DR. MC CULLEY: Dr. Van Meter, would you like to make a motion?

DR. VAN METER: I would recommend that this PMA be approvable. We have one condition, and that is that the main wound size be noted in the labeling as being 3.9 millimeters plus or minus two standard deviations.

DR. MC CULLEY: Is there a second?

DR. SUGAR: Second.

DR. MC CULLEY: Discussion of the motion?

I will call for the vote. All in favor of the motion as stated, please raise your hands high.

[All hands raised in favor.]

DR. MC CULLEY: A unanimous yes vote. We now will ask each panel member why you voted as you voted. We will start with Dr. Wang.

DR. WANG: I voted for approval with the conditions stated.

DR. MC CULLEY: Now state why you did.

DR. WANG: I feel this lens, based on the clinical trial, has demonstrated sufficient safety and efficacy.

DR. MANNIS: I voted approval on the basis of a good demonstration of safety and efficacy.

DR. MATOBA: I voted for approval. I feel that

this PMA did demonstrate adequate safety and efficacy. I do, however, still have some concerns about the haptics.

DR. GRIMMETT: I voted approval because the PMA cohort demonstrates reasonable safety and efficacy.

DR. MC CULLEY: Point of clarification, the panel voted approvable with condition.

DR. BULLIMORE: I voted approvable with conditions. I believe it is safe and effective.

DR. SUGAR: I agree.

DR. PULIDO: I voted approvable with conditions. My reserve was the concern about haptic breakage, but apparently that has been taken care of in bench studies, so I have no further problem with it.

DR. HIGGINBOTHAM: I voted approvable with conditions, because the data presented did, very nicely, reinforce or reaffirm the fact that this lens is safe and effective.

I would suggest reconsideration of the deletion of glaucoma patients and glaucoma surgery from the labeling, since the practice of medicine these days does suggest that there are a number of combined procedures being performed.

DR. JURKUS: I voted approvable with conditions because the data seemed to show that it was safe and effective.

DR. MACSAI: I voted for approvable with conditions because the data provided by the sponsor on this IOL provides reasonable assurance of safety and efficacy.

DR. VAN METER: Approvable with conditions because I believe the sponsor demonstrated adequate safety and efficacy.

I think it is helpful, when we have over 400,000 lenses worldwide implanted, that we can draw from that experience. The sponsor did a nice job in the presentation.

DR. FERRIS: I voted approvable with conditions for the reasons outlined by others, demonstrating safety and efficacy.

I would like to note for the record that, despite some of the discussions about the difficulty of doing follow up, was able to lose only three or four percent in one year.

DR. MC CULLEY: I would like to thank the sponsor, FDA and the panel for a job well done. That concludes our discussion and motion, recommendation on this PMA. It was 990014.

We are ahead of the written schedule. We are going to take advantage of that. Summit is the next sponsor. Summit will be prepared to begin early, I am told.

Let's take a 30-minute break for comfort, and for Summit to begin their presentation at 11:00.

[Brief recess.]

DR. MC CULLEY: Before we start, the tentative plan, making best guesses at how time will go, is we will have sponsor present, and we will ask sponsor questions, and then break for lunch. I reserve the right to alter that, but that is the tentative plan at the moment, making tentative guesses at what will take how long.

I would like to reopen the meeting with the discussion of PMA P930034/S13.

AGENDA ITEM: PMA #P930034/S13.

DR. MC CULLEY: I would like to invite sponsor to come forward to make a 60-minute presentation of their PMA.

DR. ANKERUD: Eric Ankerud, Summit Technology. Good morning, distinguished members of the Ophthalmic Devices Advisory Panel, FDA colleagues.

Ladies and gentlemen, I am Eric Ankerud, vice president of quality, regulatory and clinical affairs for Summit Technology, a manufacturer and marketer of eximer lasers for ophthalmic surgery.

Summit is pleased to present to you today the clinical findings for myopia and myopic astigmatism from the CRS LASIK study using the SVS Apex Plus Eximer Laser Work Station.

We are proud of the collaborative work with CRS

Clinical Research, that was instrumental to the assembly of this PMA application.

Summit's presentation of the clinical findings supporting supplement 13 to PMA 930034 will proceed as follows.

Dr. Charles Casebeer, chairman and founder of CRS Clinical Research and senior medical monitor for the CRS LASIK studies, will introduce the CRS LASIK study and review the study's evolution.

Next, Dr. Guy Kezirian, study coordinator for the CRS LASIK study, will present the study design and clinical results.

Next, Dr. Dan Durrie, director of refractive surgery at the Huntler Eye Center, medical monitor and principal investigator for the CRS LASIK study, will discuss results and provide conclusions.

Summit believes that the data to be presented today consists of valid scientific evidence supporting our requested indication for use, and that use is specifically noted on this slide: a myopic range of 0.0 to -14.0 diopters, sphere with astigmatism in the range up to -0.5 diopters.

At this time, I am pleased to introduce our next presenter, Dr. Charles Casebeer.

DR. CASEBEER: Ladies and gentlemen, Mr. Chairman, I presented to you yesterday essentially what I have to say today. It is literally the same information.

I am happy to do that, if you like, or in the interests of time, I can summarize just a little bit about the Summit study. Your choice, sir.

DR. ROSENTHAL: That is your decision, Dr. Casebeer.

DR. CASEBEER: My decision. I tell you what we do, then. I don't want to take your time unduly. Let me just refresh your memory, that we are a private research company that has been trying to help LASIK in cooperation with the FDA, to become legitimized and to validate the use of the current technology.

Although we did not expect to have an opportunity to be involved in a PMA, we are very grateful to Summit for allowing us to provide them the information in their quest for one.

The goals are clearly to work with safety issues, discourage unproven application of technology, and to try to validate LASIK to the interests of all of the physicians and all of the public, specifically by using a simple study that is easily done in the office, and by allowing the investigators to be typical of the mainstream of American

ophthalmology.

Today, we are helping Summit provide you the data for what we call approved range in substudy A. As I think you all know, we are in the process of pursuing other research endeavors for hopefully future benefit. We think it is adequate and we thank you very, very much for your attention.

DR. KEZIRIAN: Guy Kezirian, the study coordinator for the CRS LASIK studies. In the same effort to avoid redundancy unnecessarily, I will summarize some of the beginning remarks.

This study had, as its inclusion criteria, patients undergoing LASIK in the correction of spheroequivalent up to -14 and up to 5 diopters of astigmatism, which was bilateral naturally existing myopia in an eye with stable refraction for the past 12 months, objectively documented either with an eyeglass prescription, previous chart examination or other objective means.

Patients were to be out of contact lenses for three days or three weeks, depending on the type, 18 years or older, and able to complete the six-month follow-up examination.

Exclusion criteria were to exclude eyes which had had previous disease or surgery and, for the operative

parameters, the Summit Apex Plus laser was used for all the eyes presented today, an important distinction.

The oblation zone with this laser is 6.5 millimeters in spherocylinders, that ablation zone, the effective zone of that will change to 5 X 6.5 millimeters at its narrowest proportion.

Fluence of 180 millijules per centimeter squared at 10 hertz, with depth restriction to leave at least 250 microns residual corneal tissue in the posterior cornea.

Fellow eye treatments were permitted on the same day, if the first eye proceeded smoothly without complications, and reoperations were not allowed until after three months.

The safety and efficacy parameters presented today are all based on single procedure outcomes.

Nomogram adjustment was permitted. You will see a little later in the presentation, they are not large with the Apex Plus laser, but still there and still necessary, and they were developed in conjunction with CRS by adjusting the overall curve of the laser correction to the individual's personal calibration factor, as has been described for you in the application document.

This protocol was frozen on January 1, 1998 for purposes of this application, and that was to allow follow

up through six months on the eyes in the data base.

The follow up examination was one day, three months and six months with an optional one-month exam. Overall, there were 24 surgeons and 20 centers and 1,685 eyes in the overall IDE cohort.

The cohort was divided into two parts, a PMA cohort and a remainder cohort, as you see here, with 1,013 eyes in the PMA cohort that was used for primary evaluation for safety and effectiveness evaluation, and a remainder cohort which consisted of 11 investigator and 672 eyes which were also submitted which had reports in the document on table 6-8, containing the last visit analysis for the eyes in that cohort that missed visits.

There were no statistical differences determined through multiple analyses in conjunction with FDA, between the two cohorts.

As we discussed yesterday, we felt it was important to reach a 90 percent accountability target at three months, and that was the reason why we did the cohort distribution.

Again, we subjected this to a rigorous analysis for any differences between the cohorts and were not able to find any differences.

You will see that the PMA cohort has, at three

months, an accountability rate of 89.6 percent, and at six months, 84 percent.

The demographic distribution is reported here. Sex distribution, there was a slight preponderance of female to male. Right and left eyes were fairly evenly distributed throughout the study.

The age distribution had a mean age of 38 years, plus or minus 9.4 years, rather similar to what has been reported elsewhere in the literature for similar studies, with a range of 18 to 64 years.

The mean attempted correction for spheres were -6.1 diopters, sphere only corrections, with a range of -1.00 to -14.70.

For spherocylinders it was a slightly lower mean sphere with a range of .25 to 4.5 diopters of cylinder, average cylinder -1.83 diopters.

The distribution of the sphere component of the refraction is shown here, with 70 eyes at 12 diopters or above in this large study.

For spherocylinders, the cylinder component is distributed here, with 42 eyes above three diopters, seven eyes four to five, and the majority of the eyes between zero and -- well, up to three diopters.

Preoperative best corrected acuity was 20/20 in 90

percent of the eyes that were under seven diopters. The remaining 10 percent were up to 20/40.

In the over seven diopter group, 69 percent were 20/20, 30 percent were 20/25 to 20/40, and one percent of the eyes were entered as protocol deviations with best corrected acuity of up to 20/60.

Safety end points are taken from the guidance, although our protocols evolved as the guidance document was generated and circulated.

Our initial protocol was not exactly -- did not exactly include these end points, but we incorporated them in subsequent protocols as we progressed.

At request to maintain standardization, we present these results against the FDA's published guidance.

Loss of two lines or more best corrected acuity, we met the target of five percent across the board, with the highest loss occurring in the greater than seven diopter group, but maintaining it for the overall cohort and each subset.

Best corrected acuity worse than 20/40 was met across the board at under one percent, with a range of .2 to .4 percent at three and six months for the overall cohort.

Haze was not encountered in this study of LASIK. Induction of greater than two diopters of cylinder in those

eyes undergoing spherical corrections only occurred at these rates well below the five percent published rate in the guidance document.

The adverse event rates for the various adverse events are reported here, also occurring within the one percent rate for individual adverse events, as is listed in the guidance across the board.

Operative complications occurred at these rates, although surgery aborted only occurred in .3 percent of eyes overall, .2 percent were aborted due to an inadequate flap and .1 percent were aborted due to lost suction. On other eyes that experienced these other complications, surgery was able to be completed, despite the existence of these observations.

Complications at three and six months are reported here, with a slightly higher incidence noted of any staining at three months, then at six months, and remembering that this is any staining, and it would include anything from a dry eye to SBK to more serious problems.

Cumulative complications, because the previous slide represents observations that occurred, and one eye may have reported three of these complications, the next slide reports the cumulative complications to give you an idea of how many eyes were involved in that list.

A total of 27 eyes were involved in that list, and the rates are 2.5 and 2.9 percent, fairly evenly distributed, regardless of refractive correction.

IOP changes at six months were a mean change of -2.1, a drop of two points, a standard deviation of three points, and you can see that the distribution is fairly normal.

No direct correlation was found, despite an attempt to do so, to be able to predict what would happen with IOP as a result of LASIK correction, or IOP measurement due to LASIK correction, despite an attempt to correlate with all of these different factors.

Effectiveness results are compared against these targets contained in the guidance. Stability outcomes for the overall cohort was fairly flat for the overall group, virtually the same curve for the seven diopters or less and for the seven diopters or more.

Stability, we observed to occur in most eyes beyond one month from the mean spheroequivalent observation.

Using the other definition of stability, how many eyes experienced less than one diopter of change, two observations.

Between two observations and spheroequivalent, we find that the less than seven diopter group meets the target

at the one to three month observation.

Between the three and six month observation, the number was 94 percent, with a confidence interval which overlaps the target of 95 percent. In the greater than seven diopter group we have less and greater stability occurring, but still reporting at 82 and 87 percent.

Uncorrected visual acuity of 20/40 or better, with a target of 85 percent, was encountered in 89 and 92 percent of all eyes at three and six months respectively. The less than seven diopter group easily met the target at both observation intervals. The greater than seven diopter group met the target at the six-month interval.

At the 20/20 level, for which there is no published FDA target, we encountered a better than 50 percent rate of 20/20 or better in eyes at less than seven diopters at both three and six months, and greater than seven diopters experienced 20/20 vision at a rate of 29 percent and 33 percent at three and six months. Overall, the rates were 43 and 47 percent.

Again, the one-day visual acuity probably accounts for much of the popularity and success of LASIK, the rapid rehabilitation to functional vision and return to normal activities.

We found that 20/20 or better vision was attained

in 36 percent of patients on the first post-operative day in the seven diopters or less group, and 87 percent of that group attained 20/40 vision or better on the first post-operative day.

The rates for the greater than seven diopter group were 15 percent at 20/20, but a remarkable 70 percent at one day for 20/40 or better in the greater than seven diopter group.

Mean refractive serial equivalent, at plus or minus .5 diopters was attained in 57 and 61 percent of eyes at three to six months, with the higher rate in the less than seven group, and the greater than seven group attaining the target of 50 percent by six months.

The one diopter target, which is 75 percent, was met across the board by six months. The only group falling short was the greater than seven diopter group, at the three-month observation.

Cylinder correction effectiveness has been requested to be presented in the ratio of the surgically induced refractive change divided by the intended refractive change; in other words, how much was desired versus how much was achieved, using a vector analysis calculation.

These results are reported here. The ideal result would be to have all the dots going on exactly 100 percent.

You can see that they all fall rather close to 100 percent, and the tendency, if anything, was to undercorrect, which would be desirable, again, rather than to switch cylinder axis.

The standard deviation of the observations was rather tight, and what we found was that they were very tight as we went above three diopters especially.

Some of this is mathematical, because the intended refractive change, as it increases, is in the denominator, and it provides your ratio to look a little bit better, but these results were quite satisfactory across the board.

Stability of cylinder correction defined in the guidance as less than one diopter of change between the two observations was 97 and 98 percent. So, cylinder corrections were rather stable.

We performed a patient questionnaire, which was administered preoperatively and three months, to offer a comparison of preoperative and postoperative symptoms.

We reported the rates for glare, halos and fluctuations in vision as requested by FDA.

We find that in the symptom of glare, the mean preoperative was 3.4 and the mean postoperative was 2.8. That represented a decreased glare at a significance level that was very significant.

What we found was that, on the mean glare symptom reported, glare actually improved for the population following the LASIK procedure.

However, we do have a fair amount of scatter, as we encountered in other studies, and I think that it is important to use a paired analysis for these, as we did in this evaluation, in order to bring that out in the evaluation of these symptoms.

Halos were reported here, the change in the symptomatic report of halos reported here, with no significant change in the mean level, and a significant bell curve that does occur, again, as we saw in the other symptom.

The mean change in halos was not significant preoperatively and postoperatively. Judged against our other forms of refractive correction that we have used in the past, the fact that we aren't significantly affecting the mean complaint of halos is seen as a significant success.

Change in the vision fluctuation, how much does your vision fluctuate during the day, is the question. The mean preoperatively and postoperatively, we see an increase in vision fluctuation postoperatively at three months, and the scatter of those observations is reported here. The

significance was found to the .001 level.

Reoperations occurred, but not in an incremental way depending on refraction. There wasn't a relationship, or a significant correlation of the amount of preoperative correction to the likelihood of having a reoperation in this series.

The effect on best corrected visual acuity is reported here, with two percent of eyes losing two lines, eight percent losing one line, eight percent gaining some best corrected acuity and eighty-two percent not being corrected.

We did find a very significant effect of reoperations on vision. All the reoperations in this vision included refraction enhancement; all of them included a second ablation.

So, we found that the second ablation was effective in improving the uncorrected visual acuity at both the 20/40 and the 20/20 level.

We also found that the mean sphere equivalent of change occurred to be very close to the targeted zero amount, and with a very small scatter, so that the reoperations were not only affected, but they appeared to be very accurate.

Dan Durrie will come up and present some

conclusions and further results of these data.

DR. DURRIE: Thank you very much. I appreciate the opportunity to address this panel on this study. I am Dan Durrie. I am a non-paid medical monitor of CRS for this study.

I have also been a principal investigator in this study. I am a paid consultant for Summit Technology and they did pay my way here.

I would like to present a little bit more on the data and some conclusions. In general, Dr. Kezirian has shown you data that meets the safety guidelines across the board, meets or exceeds those guidelines for safety, and also has shown you data that meets the efficacy guidelines, the targets that have been set by the panel and are published, for the data that was presented.

Also, the stability was shown to be established by three months and confirmed at the six month visit in the below seven diopter range.

The stability was lower in the above seven diopter range, as expected for the larger corrections, and has been clinically acceptable.

The one thing that I have appreciated as medical monitor of the study is that there has been very small nomogram adjustments with this laser.

That is nice, when an investigator calls me and asks me where to start, and I don't have to make a lot of adjustments and a lot of calculations.

If we look at the data with no nomogram adjustment and look at it, you can see that there was a trend to overall over corrections.

Because this was a group of physicians working together and nomograms was one of our goals, we did encourage nomogram adjustment.

With the nomogram adjustment, we were able to adjust the overall scatter to less tendency to overcorrection and more tendency to undercorrection, just to protection our patients.

Especially at the time that this study was done, there were no hyperopic ablations available to go that direction. So, we did make that adjustment for safety.

I would like to look specifically at a group of eyes that are greater than 12 diopters and greater than or equal to 14 diopters in this study.

This study has 43 eyes that are in this range. Looking at their data individually in this group, at six months, no eyes lost two lines or greater of best corrected vision.

No eyes had best corrected vision less than 20/40,

and it is also interesting to note that the retreatment rate in this group was no greater than the average for the overall population.

Also, if we look at the efficacy in this group, 89 percent of these patients were 20/40 or better, well exceeding the guideline, a very acceptable percentage within half a diopter and exceeding the guidelines in the one diopter.

These patients, I think, have done extremely well, although I very much adhere to the 250 micron residual criteria.

These patients have to have thick corneas to be in this range, but those patients who did qualify did get excellent results.

Also, in this study, if you look at the division between the PMA cohort, and if you add back the remainder, which brings you to 1,685 eyes, and look at the accountability at three months and six months, although 90 percent of the patients at three months in the PMA cohort were accountable, 86 percent were countable if you put ever ready back in.

Also, if you look at the six month level, it exceeded 80 percent in all the series we put all the eyes back in, in accountability.

Now, if you look at that then and look at the guidelines again, if you put the PMA cohort and the remainder together, it does meet or exceed all of the published FDA guidelines for targets in this range, for both safety and efficacy, if all the patients are added back in.

Therefore, I think this data presented in this PMA application provides a reasonable assurance that the safety and effectiveness has been demonstrated for the indication.

I think the indication you use for this device should be in a range as previously stated, from zero to 14 diopters of sphere and up to five diopters of cylinder, if the patient meets the inclusion candidates of a stable refraction over 18 years old, and also that meets the minimum guideline of 250 microns of residual cornea. Thank you very much. That concludes the sponsor's presentation.

DR. MC CULLEY: Thank you for a very nice presentation. I appreciate it. We will now open the floor for panel members to ask questions, if you guys would like to come back to the table. Dr. Bullimore?

DR. BULLIMORE: I have a couple of technical questions I just want to have clarified, if that is possible.

When you are talking about the ablation zones for spherocylinders, you gave a zone of five millimeters by 6.5

millimeters. Is that constant, regardless of the sphere and cylinder power?

DR. DURRIE: In this study, it was across the range of cylinders. Across the range, it was the same for all the cylinders.

The way the Apex Plus laser works, with the emphasis disc, the short axis is fixed at a minimum of five millimeters, or at five millimeters.

DR. BULLIMORE: So, how does it produce an astigmatic correction that is different for a four diopter cylinder from a one diopter cylinder, if the geometry is fixed on the minor and major axes?

DR. DURRIE: It has to do with the transition zones.

DR. BULLIMORE: Another, again, technical question. You define, on your penultimate slide, stable manifest refraction as being plus or minus one diopter over the past year.

That seems, from my memory, to deviate from the guidance document.

DR. KEZIRIAN: That is what we described and that is what was included in that protocol. Our first protocol with this study predated the guidance, and that was not changed, despite the fact that the guidance came out,

because it was felt to be adequate.

DR. BULLIMORE: A comment for colleagues to discuss in a minute. I think maybe we should have the indications indicating plus or minus half a diopter as being a stable refraction. I don't regard plus or minus one diopter as being a stable refraction.

I am talking about indications for use which refer to the preoperative refraction and the stability of the preoperative refraction.

The sponsor's requested indications for use, their definition of a stable refraction is plus or minus one diopter in the year prior to the LASIK being performed.

In the guidance document and I think everything else we have adhered to previously, that I am not allowed to talk about, is plus or minus half a diopter.

DR. MC CULLEY: I think sponsor answered they began this before the guidance document came out.

DR. BULLIMORE: This is their requested indications for use. That is not their entry criteria into the study.

DR. MC CULLEY: That we will have to get into with FDA. That becomes a labeling issue.

DR. BULLIMORE: One other question regarding the astigmatism data, you presented on the slides showing the

ratio of SIRC over IRC. In the spherocylinder group, what was the mean preoperative cylinder and what was the mean postoperative cylinder at, say, three or six months, if you can call up that data. I would be grateful. I am done for the moment, Mr. Chairman.

DR. MC CULLEY: How long is it going to take you to call that up?

DR. KEZIRIAN: We just have to find the page. We will find it in just a moment. If you would like to move on, we will locate it.

DR. MC CULLEY: That is my question, whether we should go to another question and we can do two things at once while you are looking.

DR. KEZIRIAN: I have the answer. In table 6-41, it actually provides the answer with a significant amount of stratification, and breaks it down based on both cylinder amount and axis.

I don't have a single number for the entire group, but I have it broken down in that way, by each preoperative correction amount.

DR. MC CULLEY: While Dr. Bullimore is looking at that, Dr. Macsai?

DR. MACSAI: Yes, I have a question. Maybe Dr. Durrie can answer it. Is this a multi-zone, multi-pass

laser?

DR. DURRIE: No, this laser is a single pass with an aspheric blend zone built into the emphasis disc.

DR. MACSAI: What is the amount of microns removed at, say, -14, -4.

DR. DURRIE: I just happen to have that one. The number of microns removed at -14, -4, is 147.

DR. MACSAI: Thank you.

DR. SUGAR: How many reoperations were there, and what were the indications for reoperation? That is, how many were refracted, how many were epithelium ingrowth or flap or no flap or other?

DR. KEZIRIAN: All of the eyes who had a reoperation had a refractive correction included in that reoperation and a minimum of one diopter, 20/40, or a surgeon/patient agreement that a reoperation was necessary, or a guidance in the protocol for the reoperation.

The reoperation rate varied from one percent to four percent across the board. It will take me a minute to give you the number of reoperations as an absolute.

DR. SUGAR: So, no reoperations were done for epithelial ingrowth or for flap or no flap?

DR. KEZIRIAN: In this series, that is the case.

DR. CASEBEER: That is correct. They were all for

refraction, none for other things.

DR. KEZIRIAN: The number of reoperations was 40 out of 1,013.

DR. BULLIMORE: Mr. Chairman, just as a follow-up on that, I notice on one of the graphs you had patients undergoing reoperation who had 20/20 acuity. That was for refractive reasons?

DR. DURRIE: I think that the indications on that, obviously, patients I don't feel should have reoperations if they have that low level, but there may have been astigmatism in those cases. I would just have to go back to the individual ones, but obviously, that would be rare.

DR. WANG: I have two questions regarding safety. There are two cases about having the grid mistakenly left in place, and the grid was mapped onto cornea. I understand that has been corrected.

Is it now physically impossible for the surgeon to mistakenly leave that grid in place?

DR. DURRIE: Just to explain a little bit, when the laser is calibrated, there is a pattern that is put inside a cassette that holds the emphasis disc, to make sure that it lines properly, and that disc has a grid pattern.

Initially, when it was designed, it could be put in and appear to be a disc to the laser, and then that was

redesigned where it can't be put into the cassette. That has been, from a manufacturing standpoint, that can't be done any more.

DR. WANG: Thank you. My second question is regarding epithelial ingrowth. You have .9 percent incidence. What is the rate of vision in the epithelial ingrowth patients, as corrected.

DR. KEZIRIAN: I could provide that answer in just a moment and look it up specifically, but if I remember correctly, there were no cases beyond traces and some were just microscopic nests. I will look that up for you as we sit here, and if I can't come up with it now, I will provide it to you after lunch.

DR. MC CULLEY: How many of your cases of epithelial ingrowth required surgical intervention?

DR. KEZIRIAN: None of them had surgical intervention for epithelial ingrowth.

DR. PULIDO: Could you open up the table 6-3?

DR. KEZIRIAN: Yes. I am at 6-3.

DR. PULIDO: What is your range of compliance here?

DR. KEZIRIAN: Fifty-four to 100 percent.

DR. PULIDO: This is interesting, because why do you expect that, considering these are probably similar

patients to other kinds of patients in other studies we have talked about before.

The compliance rate here is markedly better. Would you say it truly is patient return that is the problem or doctor follow up, and doctors saying that to follow up, it is really important in these cases?

DR. KEZIRIAN: In this study, not only did we see that it was dependent on the surgeon itself, our 54 percent was because one of our surgeons moved to another location. So, the lowest one really had to do with the center.

I feel -- and we have had this discussion before -- that I can look at it on either side. Either the patients that didn't come back are seeing so well that they didn't come back, or I can look at it that they are doing so poorly that they went to another doctor.

I think that argument really can be balanced out on either side. I think that the compliance, especially in this type of study, in my opinion, is really dependent on what kind the investigators are doing on the sites.

DR. PULIDO: The other question that I have -- oh, first of all, I would just like to say thank you for better compliance and probably better choice of people who would make your people comply.

Table 6-2, I don't understand this table very

well. Target S, Target C and Target SE.

DR. MACSAI: Target sphere, target cylinder.

DR. KEZIRIAN: Could you repeat the table number or the page number?

DR. PULIDO: Table 6-2, page 181. Why were these patients excluded?

DR. KEZIRIAN: I didn't belabor the point today, but in the data site entry system, there were these range filters that we talked about yesterday that would have excluded entry errors such as preoperative refraction errors such as preoperative refraction of 100 instead of 10.

It wouldn't have excluded things like inappropriate data entry for forgetting to leave out a minus sign, or enter a minus sign.

So, we developed a series of queries to go through the data base as part of our maintenance program, to look for eyes that had errors.

These were the ones that were in the active basket at the time when we froze the protocol, and hadn't been corrected yet at the investigator site.

We couldn't intervene and do that. We had to have the investigator do that at the source with an audit record. So, these are the ones that were still active and undergoing the monitoring and existed for that reason. Now,

what was your specific question on this table?

DR. PULIDO: So, the target spherical equivalent was +4.25, and because you thought that was ludicrous, you excluded that?

DR. KEZIRIAN: We knew that hyperopic targets were not intended and all of these eyes went back to the surgeon's practice for re-entry.

DR. PULIDO: Did you have any further data on these eyes? I guess you can't even submit it, we can't discuss it today. Never mind.

DR. KEZIRIAN: We provided all these tables just to have full disclosure of everything that we did in the process of preparing the application.

DR. MACSAI: Dr. Kezirian, so you mean where, for example, it says target C, target cylinder of nine. That is inadvertently flipped. That is supposed to be sphere and then the cylinder of one.

Somebody transposed them, and then your monitoring program pulled them out? Did I understand you correctly?

DR. KEZIRIAN: Yes, that would be correct. You know, looking at that, I would assume they meant to hit the zero and hit the nine or something like that. I don't know that; I can't assume that. So, we have to go back to the investigator for re-entry before we can use the data.

MS. MORRIS: I wonder if you could just explain to me. I am having trouble understanding. In the presentation, although it is a small amount, it does show that there are some changes for the worse on glare and halos.

Yet, in the patient information booklet it says, the following complications were not reported, and it lists them, on page 11 of the patient information handbook.

DR. ANKERUD: The patient information booklet is still under review and would not be finalized for inclusion of complication rates and adverse events until the FDA completes its review of the clinical section from the PMA.

At that time, the actual complication rates, adverse events, would be put into the patient information booklet.

MS. MORRIS: I mean, this to the patient is a very clear statement that there are none reported. I would hope that that would be changed.

DR. MC CULLEY: Why would there be a draft that would be frankly wrong.

MS. MORRIS: This is very clearly wrong. There are reported cases. This says, the following complications were not reported in the clinical studies and it lists them.

DR. MC CULLEY: Even though your booklet may not be completed, it should be accurate as it is in draft.

DR. ROSENTHAL: The patient and the physician booklet are very carefully looked at, after the clinical data has been analyzed.

I can assure the panel that there will be very strong warnings and issues about the potential complications from the use of this device. Sometimes it is not as carefully looked at prior to the panel meeting, because we want to be sure that the clinical data is satisfactory. I apologize.

MS. MORRIS: I trust you will change it.

DR. MC CULLEY: We rely on your thorough follow up. Other questions for the sponsor?

DR. WANG: Regarding the question of 250 microns, and that is obviously more of a question of high range correction, it was in the lifetime of this study when the 250 microns became gradually more and more apparent to ophthalmologists performing this procedure.

Were indeed all the high myopic correction patients in this range, did they all have preoperative, and the 250 microns was still observed in every case?

DR. KEZIRIAN: Absolutely.

DR. MC CULLEY: Other questions for sponsor? We can ask sponsor to step down from table. Thank you.

How long is the FDA's presentation? I would like

to ask the FDA to come forward to make its presentation.

DR. BEERS: Hi. I am Everette Beers. I am acting branch chief for diagnostic and surgical devices branch. I am acting for Morris Waxler. I am going to turn this over to Jan Callaway, the team leader for this PMA.

MS. CALLAWAY: Good afternoon. I am Jan Callaway, the team leader for the Summit PMA for the SVS Apex Plus Eximer Laser Work Station.

Summit Technology, Inc., of Waltham, Massachusetts, submitted this application, which was filed on February 11, 1999.

The sponsor is requesting approval for LASIK for the correction of myopia between zero and -14 diopters, with and without astigmatism corrections ranging from .5 to 5 diopters.

The primary panel reviewers for this application are Dr. Joel Sugar and Dr. Ming Wang.

The panel input is required in this area, because clinical judgement is required to evaluate the data. Your comments from the discussion today will help us in evaluating the safety and efficacy of the device for this indication for use.

The FDA team evaluating this PMA included the following reviewers: for engineering and operators manual

labeling, Ms. Quynh Hoang, for patient information labeling, Ms. Carole Clayton, bioresearch monitoring was supervised by Dr. Jean Toth-Allen, statistic reviews were done by Mr. T.C. Liu, and clinical reviews were done by Mr. Bernard Lepri.

I would like to thank these team members for the outstanding job they have done in the review of this document.

At this time, I would like to introduce Mr. Bernard Lepri, the clinical reviewer for this application.

DR. LEPRI: Good morning again. Panel members, FDA members, industry representatives, once again I am going to present to you some supplementary information and my comments will be even briefer than yesterday.

The device under consideration for PMA P930034/S13, LASIK for myopia and myopic astigmatism by Summit Technology, is the SVS Plus Eximer Laser Work Station, Apex Plus, with emphasis disc.

These were the details of the investigations. You remember it was a six-month investigation under an approved IDE for CRS Clinical Research, Incorporated.

The first question under consideration is, do the clinical data in this PMA provide sufficient patient follow up of LASIK for the correction of myopia, with and without

astigmatism.

The review of the stability data, the stability was calculated for the entire length of the investigation, for all refractive categories identified in this PMA, including all eyes, spheres, spherocylinders and cylinders.

The stability data you are viewing on the screen was for those eyes consistently represented at all post operative visits specified in the protocol.

These are paired visits between the one and three month interval and the three and six-month interval. The mean differences, standard deviations and the 95 percent confidence intervals for the proportion of eyes demonstrating the change in manifest refraction, spherical equivalent of less than or equal to one diopter. I will give you a moment to look at those equivalents if they are of interest to you, and here is the data for the three to six-month interval.

Question number two will be, what are the panel's recommendations regarding the sponsor's presentation of stability data for LASIK and the stability ranges indicated in this PMA.

You have seen the stratifications for the one diopter units of sphere and cylinder. I would like you to take note that in the category of 10 to 13 diopters, there

are 43 eyes in sphere, and for sphere of 14 to 15 diopters, there are seven.

For cylinder, there are 35 in the three to four diopter range and seven in the four to five diopter range.

Stratified analysis of the spherocylindrical corrections for the three to four diopter cylinder range, 3.5 percent or 35 of 1,013 corrections, ranged anywhere from one diopter of sphere to less than or equal to 12 diopters of sphere.

For greater than four or less than or equal to five diopters of cylinder, 0.7 percent or 7 of 1,013 spherocylindrical corrections range, occurred only in the range of 3 to 10 diopters of sphere.

This was presented by the sponsor, 86.8 percent in the less than seven diopter category were within one diopter of MRSE, and 74.6 percent in the greater than seven diopter category were within one diopter of manifest refraction spherical equivalent.

These were the comparisons, at three months for MRSE within one diopter, so you can view the numbers in the higher diopter categories.

This is for the greater than seven diopter category at six months.

Question three will be, do the clinical data in

this PMA provide reasonable assurance of the safety and efficacy of LASIK for the correction of myopia with or without astigmatism, in the ranges indicated.

The sponsor presented their description of how they arrived at the adjusted nomogram. It is from the CRS LASIK investigation, so I won't reiterate that for you.

The same suggested labeling is present.

The programmed amount indicates the average correction that can be anticipated, but actual use may require individual adjustments of this amount. Tracking of clinical outcomes is recommended.

Question four will be, what are the panel's recommendations regarding the data on the individualized nomogram used in this investigation of LASIK.

Number five, does the panel recommend including warnings in the labeling regarding post-LASIK corneal ectasian. That concludes FDA's comments.

DR. MC CULLEY: Questions for FDA? I would like to ask again that you state for us what the device is that is being considered.

DR. LEPRI: The device under consideration is the SVS Plus Eximer Laser Work Station, Apex Plus, with Emphasis Discs.

DR. MC CULLEY: No comment about microkeratome?

DR. LEPRI: Only one microkeratome was used in the investigation.

DR. MC CULLEY: So, it would be for any approve microkeratome use?

DR. ROSENTHAL: The device, as I understand it, will be the Summit laser plus the microkeratome, with specific specifications for the microkeratome.

DR. MC CULLEY: The Summit laser with specific specifications for the microkeratome.

DR. ROSENTHAL: Correct. Is that correct, Everette?

DR. BEERS: That is correct. The specifications will be generic specifications. They will not be for any specific microkeratome, but there will be specifications, yes.

DR. MC CULLEY: Again, it is not a serial numbered or serial numbers Summit laser, it is all Summit lasers and specifications on microkeratome that are not specified.

DR. ROSENTHAL: The microkeratome must meet certain specifications.

DR. MC CULLEY: So, that is the device under consideration.

DR. ROSENTHAL: That is correct.

DR. MC CULLEY: Thank you. Other questions,

Dr. Wang?

DR. WANG: I just want to follow up. I want to clarify that for myself. To FDA, if an investigator or a physician in the future used the same laser, but a different microkeratome, a different manufacturer, is that considered FDA approved?

DR. LEPRI: Microkeratomes are non-classified. They are class I devices and they would be approved devices already on the market.

It would have to meet the generic specifications that would be placed in the labeling. That is what would be recommended. That is my understanding.

DR. WANG: So, if it has the same capability as this particular microkeratome, they would be considered FDA approved.

DR. LEPRI: Correct.

DR. MANNIS: Could you give me an example of the kind of specifications that you are talking about, generic specifications?

DR. LEPRI: We would be talking about the diameter of the flap size, flap thickness, et cetera.

DR. MC CULLEY: Other questions for FDA? Seeing none, you may retire. Don't go too far, though.

There is a sentiment that we continue to work

through. We need to determine whether that is a vocal minority or the majority. How many on the panel would like to continue to work through? How many would like a lunch break? Is that acceptable to sponsor? Raise your hands if it is acceptable. Thank you. Sponsor unanimously says yes. Truly only one wimp in the crowd.

Let's go ahead with our primary reviews. Dr. Sugar is going to be our scribe for purposes of this PMA. Dr. Sugar, would you give us your primary review?

DR. SUGAR: I appreciate the hard work that the sponsor and the FDA did in presenting this very nicely, and especially the work of Dr. Lepri.

I don't really need to review much of the data. Using the exclusion of sites with less than 85 percent accountability, the included 1,013 eyes had an accountability at one day of 99.7 percent, at three months of 89.6 percent, six months at 84 percent.

The sponsor just mentioned that when they put the two groups together, the accountability at three months was 86.6 percent and, at six months, 81.3 percent.

We discussed this issue at very great length yesterday, and I don't think it needs to be reviewed, but I think that the exclusion of sites that did badly is not an appropriate way to present data, either badly in

accountability or in any other regard.

The efficacy was high, but was dependent on preoperative refraction. At three months, uncorrected acuity was 20/40 or better in about 94 percent of those less than or equal to seven diopters. It was a little bit higher for spheres than for spherocylinders.

For eyes greater than -7, this dropped to about 81 percent. When stratified, still, this exceeded 85 percent for eyes greater than -7 up to -10.

In the -10 to -11 group, this dropped to 75 percent, -11 to -12, 67 percent, -12 to -13, 77 percent. Then, for those greater than 13, up to 14, it was only about 43 percent.

The sponsor just presented the combined 12 to 14 data and said that at six months -- this was a three months -- at six months, this was 89 percent.

The question we have is whether, I think, to set a cut off for approval at -13 or all the way at -14, and I think we need to discuss that. The data certainly were better up to -13 than they were from -13 to -14. There was only eye treated with greater than -14.

Predictability was appropriate in all groups. It appears to me that all the data is non-cycloplegia data. There was not cycloplegia data presented.

For the cylindric corrections, for patients from zero to three diopters, 83 percent ended up with one diopter or less of cylinder at three months and, for those with greater than three diopters, about 78 percent had one diopter or less of astigmatism in three months.

These numbers improved at six months to about 90 percent and 85 percent. The magnitude of surgical induced refractory correction over intended refractive correction ranged from 102 percent to about 89 percent, I think all good outcomes.

Stability was also appropriate with mean changes in cylinder, well within the guidelines and well within what are the degrees of correction that were sought.

The safety at three months, 1.4 percent lost two or more lines of best spectacle corrected visual acuity, and at six months, this was 1.9 percent.

Only two eyes at three months and three eyes at six months were worse than 20/40 best spectacle corrected acuity.

Spheres did slightly better than spherocylinders, and for spherical equivalents greater than -7, this was 2.4 percent. That is the loss of acuity was greater, the higher the correction, and I think that should be reflected in the patient information as well as physician information

booklet.

Greater than two diopters of increase in cylinder was seen in 1.4 percent in three months and one percent at six months, again, well within the guidelines.

Haze was not a problem. Over-correction of greater than one diopter occurred in 4.2 percent, and greater than two diopters in 0.7 percent.

The patient information booklet, I believe, states that one percent or less had induced astigmatism. I think that is inaccurate. I assume that they meant induced astigmatism of greater than two diopters, but that should be specifically stated, and I think that the number of one diopter over corrected at four percent should also be specifically stated.

Adverse events were reviewed and were mostly intraoperative problems, most of which did not preclude doing ablations and did not affect final outcomes.

Interoperative pressure was not a problem. Flap wrinkling occurred in nine eyes at three months and seven eyes at six months and was more common with the higher attempted corrections, as expected.

The two cases that had Xs stamped on their corneas by the machine were talked about, and that has been corrected.

We don't know what the final outcome was on those patients, although that is probably not relevant to our decision.

Patient symptoms, Lynn Morris mentioned the fact that these need to be more specifically stated in the patient information booklet.

Impressively, halos, while they increased, severe halos decreased from preop to six months. Fluctuations in vision, in the original presentation, appeared to not be a problem in more patient post-op than preop, but from the bell curve presented, there was a slight increase in visual fluctuations, and this should be mentioned in the patient information booklet.

The data present support approval of this proposal with the conditions mentioned. The upper limit of treatment needs to be discussed and the patient and physician information booklets need to have a great deal of specifics added to them, including outcomes at specific diopter ranges, and the over-corrections need to be mentioned more specifically, as I mentioned before. That ends my presentation. Thank you.

DR. MC CULLEY: Thank you, Dr. Sugar. Dr. Wang, if you could present what is different and new in your review.

DR. WANG: Ladies and gentlemen, I appreciate the opportunity to present my review, and also I would like to commend the sponsor for presenting a very well-done study.

I am just going to focus on five points that I would like to specifically mention, without repeating all the information presented already.

The first point I would like to discuss, there are a few pockets in the data which actually did not meet FDA guidelines.

The second question, there is a need to clarify the safety guideline, number one, which in fact, I will show you there are three different definitions. The sponsors have two and the FDA has a different third one.

Three, the high end falls off, which Dr. Sugar already mentioned, so I will not go through the high range corrections, due to the small number of Ns.

Number four, I will discuss very briefly about nomograms, and basically in support of the approach.

Number five, I will present specifically a literature review, and make discussion on the mechanics of the cornea regarding the 250 guideline.

I will not go through these data again. These all meet the FDA guideline.

I would like to bring your attention to what was

circled right here. This is stability for less than seven diopter. The FDA guideline is 95 percent.

There are three categories in the CRS study which fall slightly short of 95 percent, but I think the difference is close enough it probably can be considered passing, in my opinion.

However, I would like to direct major attention to this particular safety guideline number one. Safety guideline number one stated by FDA, loss of more than two lines of best spectacle corrected visual acuity, FDA specifies has to be less than five percent of the patients.

There are three ways of interpreting this. FDA says, loss of more than two lines BSCVA. CRS presented two types of data, which depending on which one you looked at, it could either meet or fail to meet the FDA guidelines.

CRS definition number one, loss more or equal than two lines best corrected visual acuity.

The second category you can look at in this context is, for those patients preop equal or better than 20/20, post-op worse than 20/25. That is a loss of over 25 with a condition preop of 20/20 or better.

So, let's look at CRS' performance. Lost more or equal to two lines best corrected, they all meet five percent.

However, if you take the second alternative definition, if you only take those patients which start out 20/20 or better and, post-op, best corrected worse than 20/25, that is a loss of over two lines, which in that sense fits the FDA guideline. They, in fact, fail four out of six. It ranges from 5.7 to 8.3 percent.

So, a comment, strictly speaking, if one were to look at this as a guideline regarding the loss of two lines of best corrected vision, in fact, there are a few pockets that fail to meet the FDA guideline.

Here a number of patients started with 20/20, worse than 20/40, one percent FDA guideline, this is 1.2 percent, integral correction range. I think that could be considered okay.

So, let's look at these three definitions and think for a moment, what is the relationship of these three definitions.

Is one definition a subset of another one? how much does it matter in the context of this PMA.

I think, looking at this particular visual diagram, this is the best way of illustrating the difference between these three definitions.

CRS, loss equal more than two lines. In fact, this largest circle encompasses the most cases. FDA guideline,

more than two lines is a subset of that, because there are patient that fall into this crescent, which is loss of equal to two lines does not fit the FDA.

If you look at one parameter the CRS study looked at, for those patients who started out better or equal to 20/20 and end up worse than 20/25, that is a subset of the FDA.

I think the point of this analysis is, one needs to be very clear in terms of safety guideline number one, what one should be looking at.

I wish CRS looked at FDA guideline number one a bit more carefully in the beginning, so that it would come up with identical study criteria. These two criteria sandwiched the FDA criteria, but are not identical.

In the category of complication, wrinkling, this exceeds one percent, but I think it is close enough.

The CRS study also studied the patient with last visit carry over. Again, the same issue arises. Again, FDA says, loss of over two lines, best corrected visual acuity, less than five percent.

CRS has two types of studies, neither of which is identical to FDAs. So, if you look at CRS definition number one, loss equal or more than two lines, in this particular subset of patients, last visit carried forward, they all

meet the five percent criteria, as double underlined here.

However, if one looks at this subset of CRS studies, in which patients start off 20/20 or better but end up worse than 20/25, that is also a loss of two lines of more.

In fact, all of the data exceed five percent. It ranges from 5.8 percent to 10.7 percent. So, the comment is, if we want to use this criteria in looking at the comparison to FDA guidelines, they in fact fail.

However, I think the point of this is probably the study itself is of fundamental merit to warrant approval with possible conditions, as a final conclusion.

However, one needs to recognize these studies differ in terms of the criteria they are looking at. I remind you that 20/20 or better at the start, those patients are 90 percent of the study.

So, in looking at this particular criteria, it is not a trivial question. In other words, this subset of patients is 90 percent of the study.

I want to use the last minute or two to discuss about two remaining issues. One is the nomogram approach and the one is the literature analysis and mechanism analysis of this 250 concept.

I think we will all take a little bit of

entertainment here. This is an easy way of understanding this personal calibration factor approach that we can use to explain to a layman patient.

I think the approach is, in principle, sound, taking into account two considerations. One, an individual surgeon has his or her own unique surgical habit, so a personal calibration factor is necessary.

However, such an approach, by globally scaling down the generic nomogram obtained from thousands of patients, the individual surgeon may not have done that many laser cases, so taking advantage of the generic nomogram based on much larger clinical series makes sense.

I just tell you a little story here. This is like an example of a referee measuring the height of high jumpers.

He measures the first jump on earth. The first jumper jumped one meter. He knows the second guy is going to jump twice as high, which is two meters, and the third, three times as high, three meters, et cetera.

Now this referee travels to the moon and he gets to measure the first jumper again. He finds the high jump of the first jumper to be six meter, because the moon to earth ratio is six to one.

Now, the point is, he did not need to measure the

rest of the jumpers. He knows that the second jumper will be 12 meters and the third, 18 meters.

There is an important intrinsic assumption, however. The moon to earth ratio, six to one, cannot change in this type approach.

To give a scenario, suppose a LASIK surgeon is a "wet" surgeon. He can put variable amounts of fluid in a stromal vat while he is LASIK-ing.

He will not be able to rely on this approach, as we have no idea of degree of hydration and ablation efficiency.

So, the point, the take home message of a caution on this nomogram approach is, there needs to be an emphasis on intrasurgeon consistency.

I think this is a labeling issue regarding humidity, temperature, all these need to be stressed to the users.

Only when surgeons consistently use the same technique, he can rely upon a consistent ratio of him or her to the generic nomogram.

Finally, I would like to discuss my literature review of the 250 issue. There are various publications published already in the literature regarding the progressive keratectasia when posterior stromal bed is left

below 250.

I just want to show you the range of posterior stromal bed that is reported in the literature. In a study by Siler et al in 1998, Journal of Refractory Surgery, there are three patients and all developed keratectasia, 177, 224 and 224.

1998, same group of authors, another patient is, in fact, above 250, 261. This study, there is no tekimetry studies, but the four eyes developed keratectasia in the high range correction, -10 over.

There is a study just reported in Ophthalmology 1999, looking at a different way of looking at the question.

Wang et al, by 32 eyes, -4 to -18 diopter LASIK correction, in looking at posterior corneal bulge, using the elevation topography, they found that if you leave more than 250, the critical number, you only have a 17 micron posterior bulge after LASIK, in the -4 to -18 diopter treatment.

If you, however, violate this critical number, you have a grossly, more than double posterior bulge, by elevation topography. So, this is a different way of looking at the number 250.

We at Vanderbilt recently had a patient, 29 years old who, after LASIK, was left 255 and 238, developed

bilateral keratectasia. This was performed over a year ago, this surgery.

This patient, 255, this patient fell short. It was only -6 treatment, however, cornea was preop thinner.

So, from a mechanics standpoint, Dreson, et al, in experimental eye research in 1980, which was also described by Siler et al in 1998, show that the tangential elastic module of keratosis cornea is smaller, compared with normal cornea by a factor of 2.1.

In those corneas, this tangential elastic module ranges from 1.6 to 2.5.

Assuming consistency of biomechanism parameters across the cornea thickness, a normal cornea thickness can be reduced by this factor before its elasticity is comparable to a keratoconus or weakened cornea.

If you take one over 2.1, using a nominal cornea thickness, that generates 250 microns. This is, in a way, a mechanical study to validate these clinical observations.

I also found an additional study just published, delayed keratectasia from LASIK.

In conclusion, I think taken as a whole this study, in this reviewer's opinion, has been well done with sufficient adequacy and safety, although there are specific conditions that we can discuss that need to be attached to

this study and it can be considered approvable with conditions. Thank you.

DR. MC CULLEY: Thank you.

DR. ROSENTHAL: I would just like to make an observation. Dr. Wang's observations were pertinent. In particular, I can assure the panel that the labeling for the device will include the issues about 20/20 and worse than 20/25, and all the factors in which there are problems, so that the patients will have a proper presentation of what the issues are that they potentially may face.

DR. MC CULLEY: I think we have been comfortable with the approach that we have taken, that the FDA has had as a panel.

I would like to open now the discussion amongst the panel, if the panel would like, prior to asking the FDA to ask its questions or, if the panel would prefer, we can go directly to the FDA questions.

DR. MACSAI: I would prefer that we go to the questions.

DR. MC CULLEY: I didn't understand your sign language. Is that the general sense of the panel?

DR. SUGAR: I would like to make a modification to my recommendation. That is that it is approvable with conditions on earth only.

DR. MC CULLEY: Thank you for that clarification, Dr. Sugar. Would the FDA please come forward and present your questions to the panel?

DR. LEPRI: With respect to the length of the investigation, question number one asks, do the clinical data in this PMA provide sufficient patient follow up of LASIK for the correction of myopia with and without astigmatism.

DR. SUGAR: Yes. I think that the yes is with the statements that have been made, that we are not happy with the compliance or the accountability when it falls below our guidance.

We don't want to give the impression that we are pleased but, in our judgement, with this particular PMA, that the accountability, with everything being taken into consideration by each member, is within an acceptable range.

DR. MC CULLEY: Is there concurrence with that? Okay, next question.

DR. LEPRI: Number two, what are the panel's recommendations regarding the sponsor's presentation of stability data for LASIK and the refractive ranges indicated in this PMA.

DR. MC CULLEY: This brings in two issues. One is stability and one is refractive range. Do you want us to

just address stability within this question?

DR. LEPRI: Just stability.

DR. MC CULLEY: Who would like to address this. Dr. Wang?

DR. WANG: Yes, mostly, but we need to caution that for high correction range, 13 and 14, as has been pointed out, the N is too small to make confident assessment.

DR. SUGAR: Are you asking us, is their presentation of stability adequate, or are you asking us to ask them to present it in a different way.

DR. LEPRI: No, the way they presented the stability data in the PMA.

DR. SUGAR: It is my feeling that the presentation assured adequate stability.

DR. BULLIMORE: I have a question. The data that was presented to us previously seems to differ slightly from the graphs that were shown today.

DR. MC CULLEY: Which data presented previously to us are you referring to?

DR. BULLIMORE: The big chunk of data that came to my office a few weeks ago and that was summarized by Dr. Lepri very elegantly today, is different from the graphs that were presented by the sponsor today.

In particular, the change from three to six months on the sponsor's graph seems to be the order of a third of a diopter or so.

Both the previously presented tables suggest that it is less than .1 of a diopter. I would like some assurance from somebody that this is okay.

DR. MC CULLEY: Dr. Lepri, can you respond to that?

DR. LEPRI: Let me go back to my slides.

DR. BULLIMORE: Dr. Lepri's slides are identical in their content to the data presented by the sponsor in their printed tables.

DR. MC CULLEY: Yet, sponsor presented slides that were different from --

DR. BULLIMORE: Yes.

DR. LEPRI: Sponsor may be best equipped to address that.

DR. MC CULLEY: Can you not deal with this?

DR. LEPRI: No, I am not familiar with the difference that he presented there.

DR. MC CULLEY: Can you make it clear to Dr. Lepri, what it is?

DR. BULLIMORE: If you go back to your tables, Dr. Lepri, slide 7. You see the mean difference there is -

.6. If you go to the next slide, which I believe is the three to six-month data, it is virtually nothing.

That is qualitatively very different from what the sponsor presented today. So, I think this is maybe a question the sponsor wants to address. They probably get the chance to address it in their five minutes of fame at the end.

DR. MC CULLEY: Do you recall what sponsor presented?

DR. BULLIMORE: The sponsor didn't present any numerical data today, but the tables that they presented to us, or submitted to the FDA and were forwarded to us in these binders, is very similar to that which was presented by Dr. Lepri.

The odd one out is the graphs that were presented today. I just want some assurance that the data is consistent.

DR. MACSAI: Can you say the name of the graph you are talking about?

DR. BULLIMORE: It is the stability one.

DR. ROSENTHAL: I think, Dr. Bullimore, this is mean difference and that is mean.

DR. BULLIMORE: I figured that one out, but the change here in all these graphs looks to be substantially

more than a tenth of a diopter.

DR. ROSENTHAL: The sponsor should address that at the end, but I can assure you that the data that was submitted is the data Dr. Lepri sent, and that is the data on which we will work.

DR. BULLIMORE: Thank you for indulging me, Dr. Lepri.

DR. MC CULLEY: So, the answer to the stability, to that question, is yes, with the consideration and concern about the higher range?

DR. BULLIMORE: Correct.

DR. MC CULLEY: Your next question?

DR. LEPRI: Do the clinical data in this PMA provide reasonable assurance of the safety and efficacy of LASIK for the correction of myopia with or without astigmatism in the ranges indicated.

DR. SUGAR: This is a little bit of a close call for the same reasons we discussed the other day, that we are getting to the tail of the bell shaped curve in terms of the ability to accrue patients in the high ranges.

Nonetheless, the numbers are low and there are seven eyes in the sphere of greater than -13 up to 14, and there are seven eyes in the cylinder greater than 4.

So, the numbers, I think, make it difficult to

draw conclusions. I think that there are two ways to approach this.

One is to approve it up to 13, where certainly the outcomes were better than in the greater than 13 range. The other would be to approve it in the full range, assuming that the numbers aren't enough to draw conclusions either way, and it is appropriate to give physicians the leeway of using the instrument in a broader range.

My own personal feeling would be that if you approve it to 14 with adequate warnings for above 13, that would allow the ophthalmic or the medical community to ultimately gain more information in these higher ranges.

The same information can be acquired by whatever techniques people have for getting around their laser's governing system, including double carding.

It we do it the way we have done things in the past, I think we should approve it up to 13. Was that a confusing enough presentation?

DR. MC CULLEY: What is your specific recommendation?

DR. SUGAR: I would recommend approving it to 14 for sphere, and 5 for cylinder.

DR. ROSENTHAL: With appropriate labeling indicating that, in the ranges from 13 to 14 in sphere and 4

to 5 cylinder there was minimum data and potentially not as good results.

DR. SUGAR: My recommendation, as before, is that the labeling include stratification by diopter in each of the ranges for both sphere and cylinder, then a warning added at the end that the outcomes are less favorable in this range and caution should be exercised.

DR. PULIDO: Point of clarification. What range on the cylinder?

DR. SUGAR: Five.

DR. PULIDO: How many were there between 4 and 5?

DR. SUGAR: Seven.

DR. MC CULLEY: Is there other discussion? Dr. Bullimore?

DR. BULLIMORE: In terms of being consistent, I would like to make a case for limiting astigmatism to 4 and I am leading toward 12 or 13 rather than 14 for the sphere.

DR. MC CULLEY: Can you tell us why?

DR. BULLIMORE: Just based on the data presented. I don't think there is enough above 13. I do think we run into, 250 microns or not, the higher we go, the more safety issues there are.

That is my gut reaction, my clinical judgement, and I think it is appropriate to go slowly.

DR. VAN METER: Mr. Chairman -- Dr. Lepri, could you please go back to graph number 14 on your slides. I think there is some information on 15 that Dr. Bullimore is probably thinking about.

Plus or minus one diopter here, above 10 diopters, it tends to fall off, according to this graph, to approximately 50 percent in the 11 and 12 diopter groups.

Thirteen and 14, the numbers are so small, as you can see, there is just one in 14. I guess I have some concerns above -12 also.

DR. MC CULLEY: Other comments? Dr. Wang?

DR. WANG: I would like to support 13. I think from 13 to 14, the number drops more sharply.

DR. MACSAI: Perhaps this is a historical perspective, but previously we have recommended cautionary language -- Dr. Pulido recommended it -- for those higher ranges, and we did not restrict that upper end.

DR. MC CULLEY: So, what is you sentiment?

DR. ROSENTHAL: Excuse me, Dr. Macsai, you have to take each PMA as it stands, and we would like your recommendation on this one, based on the data that was presented.

DR. MACSAI: I would agree with Dr. Sugar, then. That would be my recommendation.

DR. MC CULLEY: We have sentiment for 12, 13, 14 on sphere. Straw vote. Fourteen as the upper limit? Raise your hands high. If you want 14, high.

[Four hands raised.]

Thirteen?

[Two hands raised.]

Twelve?

[Four hands raised.]

All right, we are now going to restrict it to 12 or 14. We have got a tie vote. I could vote, but I choose to do it this way if I can do it this way. We are going to vote between 12 and 14. Fourteen?

[Five hands raised.]

Oh, you rotten people. Twelve?

[Four hands raised.]

Okay, so I am off the hook. So, 14 is soft and understand, folks, we make recommendations to the FDA, so they get a soft recommendation.

Cylinder, the issue is four or five. All in favor of five, raise your hand?

[Five hands raised.]

Four?

[Five hands raised.]

Okay, hands high for five for cylinder.

[Five hands raised.]

Four?

[Five hands raised.]

It is five for four. My impression is that it is difficult to get patients in these higher ranges, and if we have small numbers that give some degree of comfort, that we should go with those small numbers. I would make this soft one toward five.

DR. LEPRI: With adequate warning for the 13 to 14 diopters and the four to five cylinders.

DR. MC CULLEY: Right, but there are not a lot of people in the population in these ranges. They have a real need and I tend to be a little bit more accepting because we have much more to offer to them.

Okay, so we have set the limit at 14 and 5, with cautionary language for patient and surgeon alike. Your next question?

DR. LEPRI: Four, what are the panel's recommendations regarding the data on the individualized nomogram used in this investigation of LASIK.

DR. MC CULLEY: I think that, to put it very simply, there are a number of things that affect the adjustment, surgeon technique, laser, both brand and individual laser, the environment in which it is used, that

can be somewhat standardized, and then there is the individual patient response.

I think that a nomogram for me in one place may not be the same as a nomogram for me in another place. So, I think those kinds of things have to be stated in the labeling.

An individual cannot lift a nomogram from someone else and use it necessarily, and have it work.

DR. LEPRI: The sponsor had recommended specific labeling that I had put on the slide.

DR. MC CULLEY: Do you want to put that specific labeling up there?

DR. LEPRI: Yes, I think it would be helpful for you to see it.

DR. MC CULLEY: And as Dr. Sugar said, what planet you are on. That is environment.

DR. LEPRI: Here it is at the bottom of the screen. The programmed amount indicates the average correction that can be anticipated, that actual use may require individual adjustments of this amount. Tracking to clinical outcomes is recommended.

DR. MC CULLEY: If we change the word from may to will probably, then that language, I would think, would be acceptable.

DR. WANG: I would suggest adding a sentence that surgeons should be aware that consistent operating conditions and technique, including humidity, temperature control, is important in order to use this approach, personal calibration approach.

DR. MACSAI: I also think the sponsor should make available to the users the information they have gotten so far from all these participants in the CRS in some sort of a chart and put together what the group's results were.

DR. MC CULLEY: I would assume that they will have a matrix nomogram provided.

DR. LEPRI: That is provided.

DR. FERRIS: I actually worried about this last night, because I was uncertain why this language seemed to be bothering me.

The fix to the language that I would like to see is not that actual use may require individual adjustments, but that actual use requires individual assessment of this amount, and that tracking clinical outcomes is recommended.

It seems to me that the sense of what we are being told is that this nomogram works on the average. What I would like to have put in here is that the individual better check this, to make sure it works for them.

DR. MC CULLEY: No question.

DR. SUGAR: What is the wording?

DR. MC CULLEY: Do we have specific wording to recommend, or do we want to let the FDA work on wording, understanding our sentiment and our concern. FDA? Dr. Rosenthal?

DR. ROSENTHAL: I think we are happy to work on the wording, Mr. Chairman.

DR. MC CULLEY: You have our sentiments and you understand the issues and the constraints.

DR. ROSENTHAL: Between what Dr. Wang and Dr. Ferris and Dr. Pulido have said, we can wangle up something. Excuse me, Dr. Wang, that was a bad pun, excuse me. You have been sitting next to me too long.

DR. LEPRI: Number five, does the panel recommend including warnings in the labeling regarding post-LASIK corneal ectasion.

DR. MC CULLEY: Absolutely. The posterior 250 microns of the cornea should not be disturbed by laser or microkeratome.

All right, are there other issues the FDA would like to bring forward?

DR. LEPRI: I have none.

DR. MC CULLEY: Are there other issues the panel would like to bring forward? Dr. Wang.

DR. WANG: I don't think this will rock the boat, but I do want to see that perhaps in the future, a little bit, particularly regarding safety parameter number one.

There are, as you see, three different definitions and the CRS company has been working on two, neither of which is actually identical to FDA's safety definition number one.

If you look at one of the CRS definitions, in fact, it fails to meet. I think it is perhaps in the communication, trying to make sure that they have a category of patients that fit exactly what the FDA's exact definition is.

DR. ROSENTHAL: Let me clarify. The guidance document was developed through a working group of the Eye Care Technology Forum in 1996.

Subsequently, the agency came up with a series of tables which we felt reflected more safety values than did the single ones or two that were in the document, in the guidance document.

In fact, to be fair to all the sponsors, they are pretty much providing us with information the way we appreciated having it, knowing that we felt that possibly the original guidance of five percent greater than two lines was a bit too lenient.

DR. SUGAR: Well, do we need to add as conditions the specific things we talked about in terms of details in the patient guidance document?

DR. ROSENTHAL: Yes, we would appreciate that.

DR. SUGAR: So, a condition would be that more specifics be placed in the --

DR. ROSENTHAL: Correct. That will happen anyway. I can show you, Dr. Sugar, but it would be nice to have it in there.

DR. SUGAR: I would like to suggest that specific detailed outcome data be provided for both surgeons and patients concerning this procedure for both myopia and astigmatism, and also for -- refractive outcomes and also patient symptom outcomes.

DR. MC CULLEY: Any other comments from panel?

At this point, I would like to open the floor again for open public comments. There are 30 minutes allotted. No more than that will be used, less can be used.

Any individual wishing to speak will be limited to five minutes. I would now like to invite anyone from the audience who would like to come forward to make comment.

AGENDA ITEM: Open Public Hearing.

MR. KWIECINSKI: Dear panel members, FDA, those in attendance, I am not a speaker at all.

DR. ROSENTHAL: Excuse me, could you introduce yourself, please.

DR. MC CULLEY: And also give what your affiliation is, any conflicts of interest, economic and otherwise, that you might have.

MR. KWIECINSKI: I am trying to. I am not real good at this, sorry.

DR. MC CULLEY: That is okay.

MR. KWIECINSKI: With knees shaking, I am Rick Kwiecinski. I paid my own way here. I have been here for two days. I have a financial interest in a number of eye companies, including this one.

My personal opinion is, it would be great financially if you did something great from this. But I am here to speak hopefully on a much higher cause than this.

I have been represented a couple times in the last two days. I am a LASIK patient and have been misrepresented quite a bit in the last two days, and I feel I should speak up and tell you something about that, fill in on some of that data.

I know, and I certainly don't have the fancy charts and that sort of thing. Please forgive me. One thing that I did notice in all the data is, it clearly shows that the surgeon expertise is very critical in this.

Yesterday morning, when we started this whole thing, I was in awe and respect of everyone here for their credentials and their intelligence. It is absolutely amazing.

Now, after today, I am just in awe of your power and I am definitely intimidated here.

As far as the data, I was a perfect case on your charts. I was extremely lucky. I went for a free evaluation one day in July last summer and the doc said, yes, you are a perfect patient, you might end up with reading glasses, but that is the extent of it. You know, go for it.

I was really lucky. I had to take off for a trip soon, so they fit me in, actually, the next day. So, I had a free evaluation one afternoon and I was going to have LASIK done on both eyes the next afternoon.

I guess I am a little bit of a chicken. I only went with one. From that, everything went fantastic. I am a high myopic patient. I don't know all the numbers, but basically, over 20/400 or so. I have lived in contact lenses for about 25 years.

After the surgery or whatever, I was astounded. It was a phenomenal thing. There were tons of halos and stars everywhere and at night time it was impossible, but

luckily, I had only done one eye. I could live with that and the doc assured me that that stuff would go away.

Well, one of the things I should tell you is the reason that I had this surgery is that my contacts were not correcting me after all those years. I was increasing in astigmatism and that sort of thing, and I could not get 20/20 vision.

Because of my lines of work, the glasses weren't going to be an option for me, so I thought the risk/reward was worth it to have this surgery done on my eyes.

It certainly was. I am ecstatic. Even with the starring, in November of last year, I had the second eye done.

I thought that was almost as great. When I left there, it was perfect. Yes, there was starring and halos, but when I fill out the form, I tell everybody how ecstatic I am. I definitely am.

I can see now and my right eye is 20/20 on the chart, and sometimes my left eye is almost that good. It really varies.

You know, all of a sudden, I have had lots of problems with that one, and I definitely have a foreign body sensation in there, the vision comes and goes in the day. I do have the halos.

It is not as easy to accommodate with the starring when you have both eyes, I found out. One thing that I can definitely tell you, the starring will go away after six months, because you accommodate. You learn things.

When you are driving a boat, and you can't see any of the lights out there and it is really important, you accommodate. You stare into a light for a little while, and without the dilation of the pupil, you can get rid of the starring for a while, until you have to stare at the bright light again.

When you drive in traffic, you stare at the bright lights. As long as you don't let your pupil dilate, you are a perfect patient.

The other way that I was misrepresented in this, and I should tell you that I have been told that luckily, my right eye, which turned out very well -- thank you very much -- that was in the study, but my left eye isn't in the study.

When I hear what we are trying to approve today, I am lost on where I actually stand. See, I am a citizen of the country here.

For me to go to a free evaluation one day, and walk in with confidence the next day to get this operation is because the FDA -- thank you -- this is the country that

is harder than any other country to get approved in.

Of course, they have looked out after me. I am an intelligent man. I read the fine print. I realized there were complications. Have you ever read the complications on some of this stuff that the public is exposed to.

My point, because I realize your time is important, I think we have a critical issue here. The fact is that the machine is not the problem. It is the use of this machine.

Unfortunately, I am in awe of your power, but I have to say that I feel sorry and forgive you for that, because of the situation we seem to be in here today.

Yesterday I heard, the train is moving. The fact is that you have less control over the train if you don't approve it, because you can't put any restrictions on it.

If we go with one and we don't go with the other, boom, we blow a lot of people's confidence in some things that may be good, and boost confidence in other things that may be very equal. I don't know.

I am just a person on the street. I am Mr. Cohort. I am Mr. Cohort, Mr. Perfect Cohort, except for one thing. I was misrepresented on these charts.

I was on these charts in two different ways. One, I was represented on those charts as a perfect outcome, and

number two, I was represented on those charts as one of the accountability problems, and I am embarrassed about that.

I tell you, when you go into the office, they say, yes, you have got starring. They say it is going to go away.

You say, well, doc, thanks, I can see. I couldn't see before. I lose my contact, I am in dire danger, because I couldn't see two feet in front of my face.

He says, well, how was the halos beforehand, and how was the starring beforehand, compared to now. I thought, should I base that on clean contacts, dirty contacts, or not being able to see two feet in front of my face.

DR. MC CULLEY: I need to ask you to wrap up, please.

MR. KWIECINSKI: Okay. To wrap it up, folks, you have given your opinion to the FDA. I am glad in this country that they get to go on their own accountability.

Hopefully, I plead, I implore the FDA to listen to all the data, and the fact is, what I see as a lack of data on a lot of this thing, I see some folks here that are stuck without data.

The fact is, we are picking on those who build the machines and we are throwing the responsibility on the

patients, and there is a big gap in between.

I heard it yesterday said, hey, even if we put that on there, they don't have to tell the patient. The fact is, what is wrong with the labeling that says something along with, this machine is only allowed to be used by those who give back 90 percent of accountability for the data, so that you folks have some decent information to go on.

The company that built the laser that did my eyes, I mean, they are way on one end. The other guy, when I walk in there -- this is the thing that blows me away -- is the fact that you realize when I go in there and I say, doc, I am not really seeing that great from my left eye and it comes and goes, and maybe in this light it is a little better, accommodation again.

He says, wait, if you put your hand in front of your left eye, you realize that you only see with your right eye anyhow. It doesn't matter.

That is kind of good, but he says, don't worry about it. I will do it again, if you want it done again, but he says, you are 42, maybe that is a little better uncorrected, because if you ever need reading glasses --

DR. MC CULLEY: Excuse me, I do need to ask you to wrap up. I have been tolerant and you have gone way beyond your five minutes. Please wrap up.

MR. KWIECINSKI: Right. My conclusion for this whole thing, that the labeling on this machine should require that whoever uses presents valid data for the privilege of using that machine and, more importantly, so that you have more factual data, is the fact that a test has to be done, a scientific test, not a little handout sheet that is the responsibility of the patient to fill out, to tell you whether starring and halo is a problem.

With the data that is being collected, nobody even spoke up here today except me, and I am scared as hell. But there were folks who spoke yesterday in the morning.

The fact is that they are a little blip on that chart, and it is very hard for you to tell at this distance how crucial a factor that is in someone's life.

Yet, I can walk to my doctor tomorrow and have him do this all over again. I implore the FDA of this country to do something for the safety of these folks and to find out this data that is needed.

Please do not protect me from necessarily the machine. I have seen other things that were safe, or protect me from me, whether I choose to have it done to correct me from 2400 to 2100. Hey, if my vision went back to 2100, I would still write ecstatic down on the survey sheet.

DR. MC CULLEY: Thank you for your comments. I appreciate it.

MR. KWIECINSKI: Thank you for the privilege of speaking.

DR. MC CULLEY: Thank you. Is there anyone else in the audience that would like to come forward to speak?

Seeing no one, the open public hearing is closed. Dr. Sugar?

DR. SUGAR: Can I go back to the session where we were making recommendations? Yesterday we made recommendations that information or warning be provided in the physician and patient information booklets concerning pupil size, and I would like that to be included in this also.

DR. MC CULLEY: You must make the recommendation based on this PMA, not because of something done in the past.

DR. SUGAR: I want to make the same recommendation that we made yesterday.

DR. MC CULLEY: Okay, is there panel agreement?

FDA closing remarks. No further remarks.

Sponsor, closing comments. Five minute limit.

DR. DURRIE: Myself and the sponsor would just like to thank you for your attention on this. As an

ophthalmologist, I want to thank all of you for spending the time in your careers to do this job that is so necessary for all of us; thank you.

DR. DURRIE: Any other comments from sponsor?

Ms. Thornton, would you please read the voting options for us?

MS. THORNTON: Just to reiterate briefly, the panel's recommendation options for the vote are as follows:

Approval, there are no conditions attached;

Approvable with conditions. The panel may recommend that the PMA be found approvable subject to specified conditions, such as physician or patient education, labeling changes, or further analysis of existing data.

Prior to voting, all the conditions are discussed by the panel and listed by the panel chair;

Not approvable. The panel may recommend that the PMA is not approvable, if the data do not provide reasonable assurance that the device is safe, or if a reasonable assurance has not been given that the device is effective under the conditions of use prescribed, recommended or suggested in the proposed labeling. Thank you.

DR. MC CULLEY: Dr. Sugar, would you like to make a motion?

DR. SUGAR: I would like to make a motion that we consider this application approvable with conditions for the ranges requested, the conditions being:

That there be warnings concerning less predictable outcomes in patients requiring higher corrections, both spherical and cylindrical;

That the nomograms be individualized with a modified statement similar to that from the sponsor;

That there be a warning that the posterior 250 microns shall not be disturbed by the laser or the keratome -- that is 250 microns of the cornea;

That we add specific outcome data concerning refractions and symptoms to both patient and physician labeling;

That there be a warning concerning possible increase in adverse patient symptoms with larger pupil sizes.

DR. MC CULLEY: Is there a second to the motion?

DR. MACSAI: Second.

DR. MC CULLEY: Further discussion on the motion?

DR. BULLIMORE: I would like to offer a friendly amendment, that the indications indicate that a stable refraction is defined as less than a diopter, or a half a diopter or less change in the year prior to the procedure.

DR. MC CULLEY: Do you accept that friendly amendment?

DR. SUGAR: Is that what the guidelines state? It is. Okay, accept that.

DR. MC CULLEY Further discussion. You can deal with it.

DR. ROSENTHAL: I am afraid I can't come up with all the answers. Apparently they are suggesting different recommendations for high and low myopia, not you, but in the past. I think we will have to look into this.

DR. MC CULLEY: We are advising, and that is our advice, if the motion passes. Is there further discussion of the motion. All in favor of the motion, raise your hands high.

[Nine hands raised.]

Thank you, nine ayes. Noes?

[No hands raised.]

So, nine ayes, one abstention. I must now ask each person to state why they voted the way they did, for the record. Dr. Ferris, it is time to start on your side of the room.

DR. FERRIS: I abstained from the vote of approvable with conditions, in part to be consistent, but also because I think that in an issue of a degree of public

health importance such as this, and where the side effects, statisticians always say compared to what.

Side effects are very important in this particular situation because the alternative has its own set of side effects, but I think they need to be compared fairly accurately with serious complications.

I believe with a follow up of missing information of this magnitude, that I can't adequately assess what that is.

However, I take the point that I am not a corneal surgeon and that one of the reasons for a panel deliberation is that you bring more to the table than just looking at the current data. So, I don't want to vote against it, but neither do I feel I can vote for it.

DR. VAN METER: I voted approvable with conditions, because I believe that with the conditions that we have attached to it, the device has been shown to be reasonably safe and effective.

DR. JURKUS: I voted approvable with conditions because I believe there is a reasonable assurance of safety and efficacy, and the information will provide useful information for the consumer.

DR. HIGGINBOTHAM: I voted approvable with conditions. Based on the data provided, I believe that

safety and efficacy, or reasonable safety and efficacy has been demonstrated.

I would also add that, in addition to enhancing the patient information book so that it reflects a realistic perspective in terms of the side effects, that those surgeons who participated in this study, as well as others, work with others in the industry to work toward developing a more sensitive patient satisfaction questionnaire, so that we can continually improve our ability to pick up complications in the future.

DR. PULIDO: I agree.

DR. SUGAR: I think I have stated my case.

DR. BULLIMORE: I voted approvable with conditions. I still have concerns about correction of myopia and astigmatism at the high end of the range, and I share some of the concerns previously expressed about more careful quantification of symptoms and patient outcomes in these and other refractive procedures and look forward to further work on that topic.

DR. MATOBA: I voted for approval with the modifications, and I echo Dr. Higginbotham and Dr. Bullimore's thoughts.

DR. MANNIS: Mark Mannis. I voted for approval with conditions, based on my assessment that the sponsors

adequately, or reasonably adequately, demonstrated safety and effectiveness.

DR. WANG: I voted for approvable with conditions as outlined. I would also like to mention that it is important to stress certain technique, training and consistency in surgical techniques in offering this procedure to the public.

I would like to also express the sentiment that I recommend to the company that, having this surgeon initiated study, and to come up with a reasonable done study in this area where this procedure has already been done on a worldwide scale, that we have some data on the market that we can look at and make some judgement.

I would also like to applaud the FDA and the panel to complete its work to fruition.

DR. MC CULLEY: Concluding remarks by Ms. Thornton?

MS. THORNTON: Before you all leave, I would just like to remind you that there are two guidance documents that were noted today in the branch updates by Ms. Boulware, the IOL guidance document and the accountability, which are up for comment.

If you can obtain a copy of those on the web, we certainly would welcome your comments on those.

I would also like to thank the panel again for another day of work and deliberations. I am sure they are going to be extremely happy to give four documents back to us, and we promise not to do that again in the near future. Then again.

The PMA documents and your notebooks and all associated documents, with all the deliberations and PMAs that we have talked about over the last two days, would you leave them? On the table now is fine, because we are not going to be back here for a while.

Thank you again, and thank you sponsor, and we will see you on the 23rd of September.

DR. MC CULLEY: I would like to thank everybody for the hard work put in. We now stand adjourned.

[Whereupon, at 1:20 p.m., the meeting was adjourned.]